STUDY PROTOCOL

PROJECT TITLE: *Partners-based HIV/PrEP services for sero-discordant couples attending antenatal care: A randomized trial to increase family-based support for PrEP adherence among discordant couples through storytelling*

Date	8 November 2019
Version	1.1
Principal Investigators	Dr. Carolyn M. Audet, PhD, Institute for Global Health Vanderbilt University, USA
Funding Agency	National Institute of Mental Health (NIMH) (Dr. Carolyn M. Audet, PI)
Location	Zambézia Province - Mozambique
Expected Start Date	1 January 2020
Expected End Date	31 December 2010
Type of Study	Randomized controlled pilot
Main objective	The overall goal of this project is to develop and assess the impact of a storytelling intervention on PrEP uptake and adherence among pregnant women.
Key words	Elimination of Mother-to-Child Transmission Male-engagement PrEP Antenatal care Storytelling
NCT Title and Number	Storytelling to Increase Family Support for Pre Exposure Prophylaxis Use. NCT04071470

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Acronyms

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
APSS	Psychosocial Support (*Apoio Psicossocial para a Saúde)*
CCR	Child at risk Clinic
DPS	Provincial Directorate of Health
EID	Early infant diagnosis
EPTS	Electronic patient tracking system
EMTCT	Elimination of Mother to Child Transmission
FGH	Friends in Global Health
GoM	Government of Mozambique
HCW	Health care worker
HIV	Human Immuno-deficiency Virus
HoPS+	*Homens para Saúde Mais* (Men for Health Plus)
MOH	Ministry of Health
MTCT	Mother-to-child transmission
PLHIV	People Living with HIV
PMTCT	Prevention of Mother to Child Transmission
PrEP	Pre-Exposure Prophylaxis
RCT	Randomized controlled trial
SOC	Standard of care
VUMC	Vanderbilt University Medical Center
WHO	World Health Organization

1. Principal Investigator

The principal investigator (PI) for this evaluation will be Carolyn Marie Audet at Vanderbilt University Medical Center (VUMC). The PI will be responsible for all aspects of evaluation coordination, including design, implementation, and analysis.

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2. Funding

This project will be funded by a National Institute for Mental Health (NIMH) supplement to a parent R01 award (PI. Audet).

3. Collaborators

Various project staff from the Ministry of Health (MoH) and Friends in Global Health (FGH)/Vanderbilt University Medical Center will be involved in this activity. From the MoH, this includes Arifo Aboobacar, an assigned member of the Operational Investigation Committee of Zambézia (NIOZ). From FGH, this includes Caroline De Schacht, M.D., MSc, Ph.D.; and Fernanda Alvim, M.P.H. From VUMC, this includes Carolyn Audet, Ph.D. and Erin Graves, BSN, M.P.H.

Table 1. Other participants in the study.

Name	Organization	Role	Role in the Evaluation
Arifo Aboobacar	DPS-Z	Operational Investigation Committee of Zambézia (NIOZ)	Collaborator; NIOZ Focal Point; Technical oversight

Caroline De Schacht	FGH	Director of Evaluations	Co-Investigator; Technical oversight; support of HoPS+ Study Manager
Fernanda Alvim	FGH	Director, Monitoring and Evaluation	Collaborator; Data Quality Monitoring
Almiro Emílio	FGH	HoPS+ Study Manager	Study Manager; Coordination and supervision of study
Erin Graves	VUMC	Senior Program Manager	Study Manager; Technical and administrative oversight
Carolyn Audet	VUMC	Principal Investigator	Principal Investigator; Technical oversight and mentoring

4. Introduction and Justification

One of the world's poorest and most medically underserved regions, Zambézia province is located in north-central Mozambique. Zambézia province is home to 4.5 million people in one of the poorest regions in the world; its people live on subsistence agriculture, the educational system is weak, and few social support services exist.[1] In 2015, adult HIV prevalence was estimated at 15.1%.[2] The Vanderbilt University Medical Center (VUMC)-affiliated non-governmental organization Friends in Global Health (FGH) supports more than 200 health facilities that provided antenatal care (ANC)-based HIV counseling and testing to 155,000 women in 2016-2017. Of those, 65% received couples-based testing. Approximately 7-10% of couples identified in ANC are composed of an HIV-uninfected person with a ***partner*** living with HIV. High rates of serodiscordant couples led the Ministry of Health (MoH) to initiate pre-exposure prophylaxis (PrEP) distribution free of charge to all serodiscordant couples in Mozambique.

B.1.1. Acquisition of HIV during pregnancy increases mother-to-child-transmission (MTCT) risk.[3, 4] The risk of HIV transmission among pregnant and post-partum women is significantly higher when compared to non-pregnant female counterparts; with adjusted risk ratios of 2.82 and 3.97, respectively.[5, 6] Pregnant women in Mozambique seroconvert at a rate of 4.28/100 women-years,[7] which is similar to published incidence data from Swaziland,[8] Uganda,[9] and South Africa.[4, 10] Among pregnant women in known discordant relationships, HIV incidence is 12.5 per 100 women years.[11, 12] In African cohorts, women with incident vs. chronic infection during the pregnancy/postpartum periods had a higher risk of mother to child transmission (OR 2.3, CI 1.2 - 4.4)[12] thus PrEP is essential to preventing incident mother and infant HIV infections.

PrEP offers a bridge to partner ART initiation[13] and viral suppression.[14] Among discordant couples, the risk of HIV transmission continues up to 6 months post antiretroviral treatment (ART)-initiation.[11, 15] The World Health Organization (WHO) recommends combining ART with PrEP for HIV-1 prevention.[16] Integration of PrEP delivery and ART initiation, decreased HIV incidence in the negative partner to <0.5% per year.[14] Recent studies of PrEP in pregnant/lactating women revealed no safety-related concerns during implementation[17-19] and PrEP is now recommended by the WHO and the U.S. Centers for Disease Control and Prevention (CDC) for use among HIV-uninfected pregnant women if their partner is a person living with HIV (PLHIV).[20] Randomized controlled trials have demonstrated that women on PrEP must maintain very high levels of adherence for the drug to be effective.[21, 22]

Family support can improve uptake of, retention in, and adherence to PrEP among pregnant/lactating women.[14, 23, 24] Women have identified a lack of support from husbands or male partners as a principal barrier to engagement in ANC and HIV services during pregnancy.[25-28] Qualitative[24, 26, 29-31] and clinical trial data[32] across sub-Saharan Africa (SSA) reveal that women are reluctant to accept HIV testing, HIV treatment, or PrEP services if their partners or families are unsupportive, highlighting the importance of programmatic adjustment to prevailing gender norms. In rural Mozambique we found that family beliefs affect a woman's health decisions.[33] Mozambique is not unique; acceptable engagement of partners in HIV counseling during ANC has resulted in increased acceptability of testing and treatment uptake across SSA.[34-42] We anticipate maternal uptake of PrEP services will face similar challenges.[43, 44] Thus, we propose a culturally-grounded, family-based approach.

Will treatment adherence by one partner result in decreased adherence by the other?
Will serodiscordant partners receive differing levels of family support (i.e. more support for negative woman or positive man)?
Do people learn more about PrEP via storytelling vs. counseling sessions?
Can family support for PrEP use overcome partner neglect or rejection? Or Can partner support for PrEP use overcome extended family neglect/rejection?

Table 2: Unique social challenges faced by serodiscordant couples

Family-based support systems are essential to changing health-related behaviors. Families, including couples, are a proven, effective unit of intervention in the African HIV prevention and care context. [29, 34, 36, 37, 39, 44-52] Our successful "Men for Health" program was designed to increase male participation in ANC services, including couple-based HIV testing. We trained "male champions" to counsel husbands about the importance of ANC uptake, HIV counseling and testing, and the need for men to provide physical and emotional support to their partners during pregnancy. Male partners were encouraged to accompany their wives to the health facility for ANC services. Traditional Birth Attendants (TBAs) were trained to provide similar education to pregnant women. We increased couples testing from 2% to 60% in less than three years.[44] While couple-centered behavioral interventions have been effective in reducing sexual and drug-risk behaviors, increasing access to HIV testing, and improving uptake of PrEP services,[29, 34, 36, 37, 39, 44-56] no studies have assessed the effect of family-centered interventions on adherence to maternal PrEP/paternal ART during pregnancy and lactation.[14]

Discordant couples face unique challenges to adherence and retention in care (Table 2). Couples in concordant relationships are more likely to stay together than those who find themselves HIV discordant. PrEP is so new to Mozambique that few people have heard of it before it is offered at the health facility. This lack of information can be exploited; stigma towards those who use PrEP is non-existent. However, the lack of information about the medication can make it difficult for families to understand the importance of adherence, the value of the medication, or the potential role they have in supporting women taking medication. As with people taking ART, family engagement can address multiple patient-reported barriers to retention in care in rural Mozambique, notably lack of partner support, challenges with transportation and security while traveling to and from the health facility, and disbelief or denial of the existence of HIV by family members.[57, 58] More so than with ART, including partners in the education, counselling and treatment process can improve male partner retention by creating accountability and support: a woman cannot stop PrEP until her male partner is virally suppressed. If both partners (and their families) understand this, commitment to treatment is enhanced.

Families cannot provide substantive support to discordant couples unless they have adequate knowledge and skills to do so. Among participants in the HoPS+ study, the average level of education is only two years. More than 50% (primarily women) have no formal education; many of these individuals do not have the ability to even sign their own name. Our R01 is situated in an extremely rural portion of Zambézia Province with little exposure to larger towns or cities. There has been a long-standing struggle to develop educational strategies to explain what HIV is, what HIV is doing in their bodies, and how medication works to improve the health of people living with HIV. Currently, counselors in our clinical sites describe HIV as a tiny bug that lives in patients' blood. The medication puts the bug to sleep, but the bug never really goes away and will wake up if the patient stops taking medication. The level of detailed understanding about the disease is not as important as the creation of a relevant construct that allows people to contextualize their illness and the interaction between their medication and disease progression. Explaining how PrEP works and developing motivational messages that are effective in this population remains a challenge. Our interviews among discordant couples revealed a complete lack of information about PrEP; they are offered it at the time of a discordant test. Development of a couple-based education and messaging is essential to improving knowledge.

People are seven times more likely to remember a story vs. facts alone.[59] Mozambique has a rich history of oral storytelling, a cultural tradition we will integrate into this intervention. Couples live with, and are influenced by, their immediate and extended families and >95% of patients disclose their HIV status to at least one of their family members (ongoing study, Audet personal communication, 2019). The strength of family support provided to the discordant couple is correlated with adherence to medication and retention in care.[60] Developing and delivering engaging stories has proved essential via numerous RCTs for several reasons: (1) Stories act as mnemonic devices for facts;[61, 62] (2) Stories engage our emotions, which results in increased empathy and adoption of messages;[63] and (3) Stories that engage participants lead to story-consistent beliefs.[64] Narratives have been used to persuade patients to accurately assess their risk of a particular condition (lung cancer, cervical cancer, etc.), in efforts to change behavior (smoking, condom use) or uptake specific medical services (HPV vaccination, lung

cancer screening).[65-69] Given the history of oral storytelling as education in Mozambique, there is evidence that this culturally-informed tradition can be used to reduce HIV stigma[70] and increase understanding of complex topics[71, 72] like PrEP and ART use.

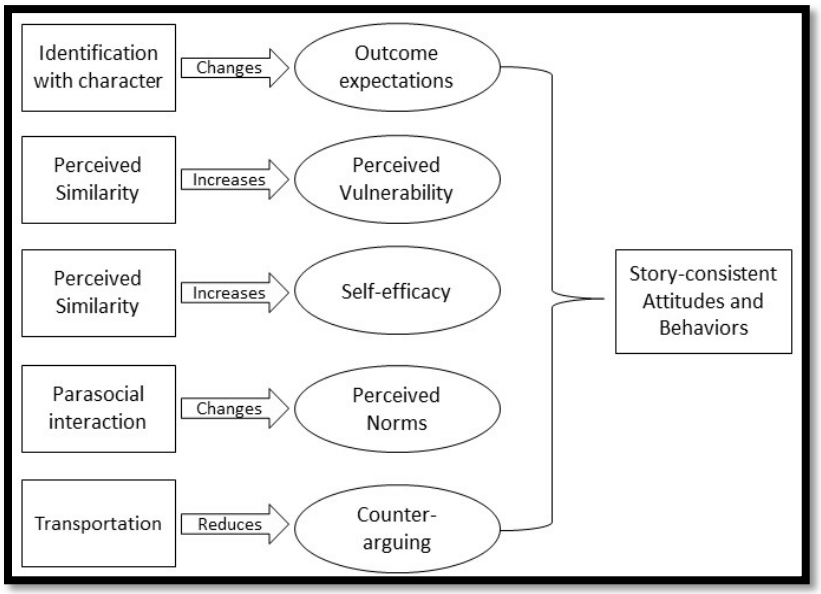


Figure 1: Impact of Storytelling

The use of entertainment-education fosters interest among listeners in the events and characters described in the story. This engagement, also described as transportation, immersion, and absorption[69] differentiates overtly educational messaging from entertainment-education. Successful narratives engender participant *involvement* with characters. This involvement occurs through five mechanisms: (1) Identification with a character or characters; (2) Wishful identification with a character (i.e. wants to be like a character but does not see themselves like that person currently); (3) Similarity with a character (e.g. physical attributes, race, values, personality); (4) Parasocial interaction[73] between the audience and narrator (i.e. the illusionary experience of friendship with the narrator); and (5) Liking the main characters of a narrative (e.g. I would like to be friends with this character). While the listener is enjoying the story, they are (ideally) identifying with a character that they deem likeable and similar to themselves; the behavior and experiences of the character becomes acceptable and appropriate to the listener.

The experiences of the character serve to motivate the listener to change their own behavior or beliefs, without generating counterarguing based on previously conceived opinions or expectations. Storytelling can influence outcome expectations among the listener (e.g. “PrEP does work to keep me from contracting HIV!”), shift a listener’s notions about their own vulnerability to HIV infection and self-efficacy to change their behavior (e.g. “If they can do it, so can I!”). The interaction between characters can change perceived social norms in relation to protective behavior and/or treatment uptake (Figure 1).

Accurately assessing adherence to medication is essential to understanding if an intervention is successful. People frequently overestimate their adherence to medication or have difficulty quantifying how much medication they took, and individuals without sufficient PrEP in their system are more likely to seroconvert than those with detectable levels of tenofovir in their urine.[74] Thus we propose to conduct a urine assay to monitor adherence in real time using disposable, point of care, qualitative tests at each clinical visit.[75]

5. Objectives

The overall goal of this project is to develop and assess the impact of a partner-based ART delivery intervention among HIV-positive expectant couples.

Our specific objectives are as follows:

Objective 1: Compare the effect of a storytelling intervention (vs. couple-based counseling) on participant knowledge, motivation, and behavioral skills associated with PrEP retention and adherence.

Objective 2: Evaluate the impact of a storytelling intervention on adherence to PrEP/ART medications.

Objective 3: Assess the experiences of participants and family members in the storytelling intervention.

6. Design and Study Questions

The proposed study is a two sample, couple-randomized pilot to test the impact of an oral storytelling intervention (versus standard of care PrEP/ART delivery) to increase retention in, and adherence to, PrEP and ART among HIV-discordant expectant couples.

There are seven specific study questions:

Question 1: Is our intervention idea acceptable to discordant expectant couples and their families?

Question 2: Does our intervention positively impact partner support for PrEP/ART medication adherence and retention in care?

Question 3: Does the intervention increase empathy among partners enrolled?

Question 4: Does the intervention increase knowledge about HIV?

Question 5: Does the intervention reduce depression among couples enrolled into the intervention?

Question 6: Does our intervention improve the proportion of exposed infants who are tested for HIV (early infant diagnosis [EID])?

Question 7: Does it decrease the number of infants who are HIV-positive at 12 months?

7. Study Population

a. Population:

1. Couples consisting of two adults 18 years or older (one HIV-uninfected pregnant woman and her HIV-infected male partner) presenting for ANC services together in Zambézia province, and their infants.
2. Family members of couples in the intervention group who participate in the storytelling events.

b. Inclusion Criteria:

1. Couples, one pregnant woman and her male partner, will be eligible to participate if: i) the male partner is identified as HIV-positive at any ANC appointment, either through ANC-based HIV testing or having a known history of HIV-positive (from clinical records or medication pick-up documents, or any other mechanism by which ANC staff identify him as HIV-positive); ii) both persons agree to take PrEP (pregnant woman)/ART (male partner) together and receive standard care in pre- and postnatal period, including care of the HIV-exposed infant ("CCR – Consulta de Criança em Risco"; iii) the woman's due date is >4 weeks from study enrollment; iv) both persons are 18 years or older; v) both persons are able to give informed consent; vi) both persons (parents) are willing to consent to an infant record search, and v) both persons consent to be in the study.
2. Family members (as defined by relatives living in the participants' household or relatives the participants identify as living in the study community) will be eligible to participate if: i) they participated in at least one of the storytelling sessions; ii) are 18 years of age or older; iii) are able to give informed consent; and iv) are willing to participate in the interview.

c. Exclusion Criteria:

1. Couples will not be eligible to participate in the study if the woman is not pregnant, if she is HIV-positive or if her partner is not HIV-positive, if either person is younger than 18 years, if one member of the couple is unwilling to enroll in PrEP/ART or consent to the infant record search, or if one member of the couple is unable or unwilling to give informed consent for any reason.
2. Family members will not be eligible to participate in the study if they do not participate in at least one storytelling session, if they are younger than 18 years old, if they are unable or unwilling to give informed consent for any reason (e.g. have been drinking or show other signs of mental limitations), or if they are not willing to participate in the interview.

d. Calculations of Sample Size:

Objectives 1 & 2: Our pilot will involve 70 couples (70 HIV-negative pregnant women and their HIV-positive male partners; 35 couples in each arm) from a single clinic. Limited data on PrEP in Mozambique suggest 55% of pregnant women were not retained at 3 months after PrEP initiation. Given our sample size of 70 women and a 5% type I error, we will have 82% power to detect a RR of 0.40 for not being retained. Should there be evidence the intervention effect is similar for men and women with regards to retention, the two groups can be analyzed together to further improve power to detect RRs closer to 0.50. We do not have estimates of Tenofovir levels among PrEP users, but other studies indicate as many as 70% may have no active drug detected.[76]

Given our sample of 70 women and a 5% type I error, we will have 85% power to detect a RR of 0.50 for no detectable drug level.

Objective 3: Interviews will be conducted with 25-40 family members and 15-20 couples who participate in at least one storytelling session four months after enrollment. We will recruit family members of at least 10 different couples to ensure we have enough variability. We will complete interviews until we reach data saturation[77]. In this population, data saturation has been reached after an average of 30 interviews; thus, we hope to reach saturation with this sample.

e. Sampling

1. [*Objectives 1-2*] Participants: Eligible discordant couples will be enrolled at the study site on a first come, first enrolled (consented) basis until 70 couples have been enrolled. Randomization will be done using Stata with the results printed into numbered envelopes opened by the study assistant at the time of participant enrollment.
2. [*Objectives 3*] Participants: For qualitative in-depth interviews with family members, we will use convenience sampling to identify family members of couples who were successful and those who were unsuccessful at adhering to PrEP/ART.

f. Recruitment procedures

Serodiscordant couples identified in ANC will be informed about their eligibility for a study by the maternal and child health nurse. If the couple is interested in discussing further, they will be referred to a study assistant based at the health facility. This study assistant will sit with both members of the couple to describe the study. The specific points they will address include (but are not limited to), (1) that if the participants are randomized to the intervention group we will include them and their nominated family members in three storytelling sessions to increase understanding and support for use of PrEP and ART medications; (2) that some people are randomized to the control group, which means that they will receive the normal PrEP and HIV care and treatment at the health facility; (3) that we will measure the female's PrEP adherence using a point of care urine test at each medication pick up for the first three months on the PrEP regimen. The couples will be offered to ask any questions and will be explained that their participation is voluntary. If the both members of the couple consent to participate, they will be randomized to the control or intervention group using a pre-determined allotment recorded within a sealed envelope at the health facility site.

Family members of intervention participants who are nominated for participation by the discordant couple will be recruited by the study assistant at the home of the discordant couple (already consented and enrolled in the study). The discordant couple will ask their family member(s) to stay home or invite their family member(s) over during a pre-arranged time slot, and the study assistant will meet them there to explain their potential participation in the trial and to obtain the family members' consent (if applicable).

g. Patient participant retention and withdrawal:

Participant retention and withdrawal from clinical care: As per standard clinic procedure, peer educators will track all patients who miss appointments at the health facility selected as study site. The peers will document patients as terminating clinical care services if they: (1) discontinued

services due to death; (2) transferred their care to another clinic; (3) are lost to follow-up (defined as being >60 days late for a clinic appointment); or (4) discontinue for any other reason, including patient choice.

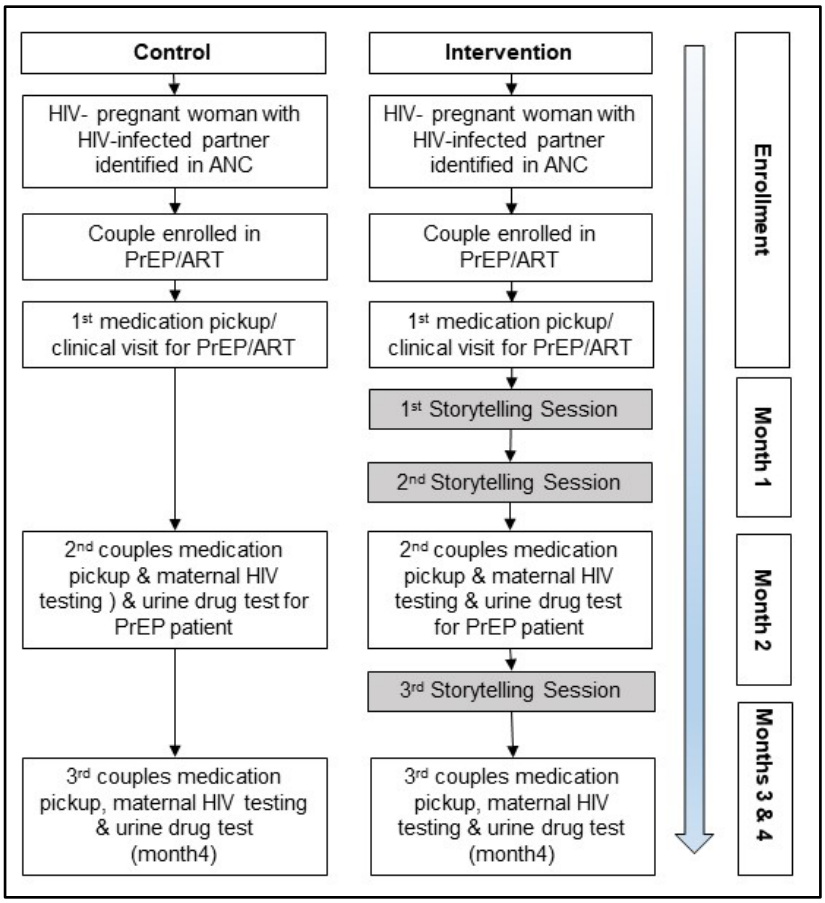
Participant retention and withdrawal from pilot: Study participants can choose to discontinue participation in the study and decide that their medical data and/or study data cannot be used in the analysis at any time by formally communicating their decision to the study manager.

8. Methods

a. Study Procedures for patients

Standard of care (SOC): The participants randomized to the control arm will receive SOC services that include: (1) standard male engagement (male invitation to ANC services and couples HIV testing), (2) opt-out rapid HIV testing of all pregnant women attending ANC, including two HIV tests before PrEP initiation to ensure patient status [Determine HIV-1/HIV-2®, (Abbott Laboratories, Abbott Park, Illinois, USA)] followed by [Unigold HIV-1/HIV-2® (Trinity Biotech Plc, Bray, Co. Wicklow, Ireland)], (3) Confirm estimated creatinine clearance (CrCl) ≥ 60 mL/min per 1.73m^2 prior to ART initiation and periodically during treatment, (4) Counseling for the HIV-positive partner as per national guidelines; (5) PrEP medications, condoms and psychosocial support (PrEP package) free of charge, and (6) follow-up HIV testing at time of medication pick-up (1 month and every three months thereafter). The partner will be referred to one of the differentiated models of care if viral load (VL) is suppressed at month 6 (at which point the PrEP regimen may also be suspended with clinician's approval). If the male partner abandons HIV care and treatment, the woman will continue to be eligible for PrEP. Postpartum women on PrEP receive follow-up at the adult clinic for PrEP services; her infant is followed at the Health Child Clinic for clinical follow-up and vaccination; if the woman seroconverts, infants have access to HIV testing by dried blood spot (DBS) PCR as early

Figure 2: Procedures in SOC vs. Intervention Arm



as six weeks after birth. If the infant seroconverts, s/he is provided ART for life. Follow-up at respective clinic points for mother and infant continues for 18 months or until the mother ceases breastfeeding. Relevant medications are also offered free of charge in the adult HIV clinic to male partners (Figure 2). If the woman seroconverts at any point during the study, HIV-specific counseling and support, provision of cotrimoxazole prophylaxis, Isoniazid Preventive Therapy, and universal ART are provided free of charge (currently all adults are offered ART, regardless of CD4 cell count).[78] Viral load testing is routinely available for all ART-treated children and adults. The only other procedure that is not considered SOC, but will be conducted with all consenting study participants, including in the control arm, is the monthly measuring of PrEP (tenofovir) drug level via urine assay testing, which will be explained to all participants prior to consenting to study enrollment. **Storytelling Intervention**: The participants randomized to the intervention arm will receive all of the SOC services and PrEP drug level testing (for female) as described above (i.e., will receive the same SOC clinical services as those couples randomized to the control arm). In addition, the individuals randomized to intervention arm will be invited to participate in three storytelling sessions with their partner and family members (of their choosing). The stories will be told by theater-trained community members who will deliver the narratives in the first person, each person playing/voicing an assigned character at the couple's home (or in a preferred location chosen by the participants). Each narrative will last 12-15 minutes. At the conclusion of the narrative, the facilitators will open up a discussion with those listening to the story. They will engage the family in a discussion, asking them about the storyline they just heard. They will ask questions to specifically probe for reactions to events and difficult characters/interactions. They will lead the discussion about ways the main characteristic (discordant couple) overcome challenges in adherence to medication; seeking to see if there are ways the messages can be related to their own lives (Appendix 2). We will conduct the first two stories in the first month of enrollment to try and influence participants' behavior/thinking prior to their first follow-up visit for medication pickup (in an effort to assess storytelling's impact on attendance at visit).

Procedures for drug level measurement.

Every time the couple returns for a medication pick up the woman on PrEP will be asked to provide a small sample (1ml is sufficient) of urine for the tenofovir assay. If a participant misses a medication pick-up, or if their male partner picks up their medication, the study assistant will bring the urine assay to the participant's home to complete the test. The test is simple to use: like a pregnancy test, the patient only has to urinate on a testing stick to identify the presence of the medication.

Study procedures for the qualitative interviews

Qualitative interviews will be conducted at least 4 months after the couple and their indicated family members have been enrolled in the study. We will purposely select roughly equal numbers of participants (including couples and their family members) who were adherent to PrEP/ART and those who have not been adherent to medication (measured via ART pick-ups and PrEP drug level assays). Interviews will be arranged by the study assistant and can be completed either at the health facility or at the home of the participant (depending on the preference of the participant). The qualitative interviews will only be completed one time, with no additional follow-up for the

participant.

Measurement of Results

Objective 1: Using interviewer assisted surveys, we will collect male and female partner (1) depression;[79] (2) partner and family support;[60, 80] (3) empathy;[81] (4) relationship satisfaction;[82] (5) PrEP adherence knowledge; and (6) motivation/perceived ability to adhere to medication[83] at baseline and three months.

Objective 2: Routinely collected demographic, community-based social support, and PrEP/HIV care and treatment data will be used in the analysis. Select demographic, clinic, and laboratory data (see Appendix 1) from these forms are entered routinely into OpenMRS (an electronic medical record "EMR" system) at FGH-supported sites. We will collect data about participant eligibility among those who attend ANC services including reasons for refusal among eligible participants. Lastly, we will assess PrEP drug levels using urine analysis (not considered standard of care) among participants in both groups (control and intervention).

Objective 3: Qualitative interviews will be measured using open-ended interview questions to understand their perspectives and experiences with the study activities, strategies, benefits, disadvantages, and suggestions for program implementation and improvement. These qualitative interviews will not necessarily provide objective measurement, but rather in-depth information regarding program implementation issues and strategies for improvement.

b. Instruments used in the study

We will use the following instruments in the study: (1) depression;[79] (2) partner and family support;[60, 80] (3) empathy;[81] (4) relationship satisfaction;[82] (5) PrEP adherence knowledge; and (6) motivation/perceived ability to adhere to medication[83] at baseline and three months (Appendix 3). These instruments are quantitative scales with closed ended response options. During qualitative interviews with our smaller samples we will follow semi-structured interview guides (Appendix 4).

c. Anticipated end date of study:

This study is expected to be concluded in September 2020.

9. Locations of Study

This pilot will be conducted at Namacurra Sede health facility.

10. Data Management and Analysis

Data Management and Security

The data collected will be kept in a database housed in Mozambique. Data will be stored in a restricted access folder that sits on the FGH server. In addition, data will be password-protected to limit access to staff involved in the study and to ensure confidentiality. Data will be encrypted,

backed up on FGH servers, and uploaded to the VUMC servers as needed for PI access. FGH servers have daily backups scheduled; therefore, all data will be backed up on a day-to-day basis.

Data from the surveys will be coded and transferred into a REDCap database by field staff trained in data entry. The original surveys will be locked in a file cabinet in the FGH office in Quelimane for five years. The interview data will be recorded; field workers will transcribe the data within a month of the interview into a password-protected Word document. After transcription and translation, the original recording will be deleted. Only the PI, investigators who will complete the analysis, and the Study Manager at the FGH Quelimane office will have access to the coded data. The data files will be password-protected to ensure confidentiality. All routine monitoring data will be documented by health facility staff into patient clinical records. Data are extracted from patient clinical records into electronic patient tracking systems already established and functioning as part of routine monitoring by FGH data entry specialists. The staff has specific training on data confidentiality; all FGH staff sign confidentiality agreements as they come into contact with patient clinical files.

As the HIV care program has grown, FGH and other PEPFAR partner organizations within the province have implemented electronic databases using either ACCESS® or OpenMRS, depending on the district, to collect patient information facilitating the maintenance of these records for the Ministry of Health's program. At the end of each patient encounter, data entry personnel based at the health facility enter information collected on the paper forms into the electronic database. This database does not have the capacity to collect information from the various different services and connect them to a specific patient. As a result, only information from the HIV care is currently collected in the electronic database.

The OpenMRS databases are password protected and can only be accessed by FGH monitoring and evaluation staff. Data quality assurance for the OpenMRS is ensured through semi-annual audits as well as automatic data validation steps. All data are reviewed by FGH regional data supervisors at the district level and by data analysis officers based in the FGH provincial offices in Quelimane. Corrective measures are taken as necessary as a result of data quality audits and regular reviews of data.

For this project, de-identified data will be extracted into a restricted dataset by FGH employees from the existing OpenMRS databases and sent to a VUMC Biostatistician for analysis. All routine programmatic data are owned by the MOH. All routine programmatic data are part of the clinical record and as such will not be destroyed.

Data from interviews will be transcribed (and if necessary translated from local language into Portuguese) at FGH Quelimane office. Transcription data will be typed up into Word documents, and subsequently translated into English. The English transcriptions will be imported into MAXQDA 12® software to be coded by Dr. Audet and a study assistant. The electronic database will be coded. The data will be password-protected to ensure confidentiality. Data will be stored in a restricted access folder (protected by an additional password) that sits on the VUMC server.

VUMC servers have daily backups scheduled; therefore, all data will be backed up on a day-to-day basis.

The original audio recordings of the interviews, which will not include participant names or other identifiable information, will be locked in a file cabinet in the FGH office in Quelimane until transcripts of the interviews have been entered into the database and the data has been checked for errors. After this point they will be erased to ensure voices cannot be linked back to the transcripts. All paper copies of transcripts will be destroyed once they have been typed up, verified, and the electronic versions have been sent to VUMC. All electronic copies of transcripts will be kept in a password-protected folder on a secure server at VUMC for a period of 7 years, after which time they will be destroyed by the PI (Dr. Audet).

Data Analysis

Objective 1: *Statistical analysis plan for Objective 1.*

Qualitative Analyses

Audio files will be transcribed verbatim by a research assistant and two researchers will code and analyze the interviews using MAXQDA® software. We will employ a thematic approach to identify and analyze themes in the data.[84] We will focus on two key reactions to the storytelling: (1) the experience of listening to the stories, with a focus on the effectiveness of the narrators ability to transport the listener, the level of identification and perceived similarity with characters; and (2) the impact of the storytelling intervention on information related to PrEP/ART adherence, motivation to adhere to medication due to self-efficacy, family support and feelings of depression/hopelessness, and behavioral skills learned. We will use a combination of deductive codes based on findings from previous adherence research and inductive codes to categorize newly-identified factors associated with uptake, adherence, and retention in PrEP/ART services (e.g. self-efficacy, partner support, information etc.). Two researchers will read through the transcripts several times and highlight relevant examples of storytelling impact on information, behavioral skills and motivation. Researchers will generate codes and highlight themes by collating codes across the data set and the review themes to develop a thematic map (e.g. the influence of a character's successful use of a strategy on a listener's self-efficacy to employ the same tactic). The final coding framework will have at least 85% agreement between the two coders. This exercise will allow us to modify our behavioral model if necessary.

Quantitative Analyses

AIM 1 Endpoints: (1) partner/family support;[60, 80] (2) empathy;[81] (3) relationship satisfaction;[82] (4) PrEP adherence knowledge; (5) depression[85]; and (6) motivation/perceived ability to adhere to medication[83]

Analyses will follow an intent-to-treat protocol. We will estimate the intervention effect on mean outcome scores using separate *linear regression* models for each outcome. If any outcome demonstrates a skewed distribution, we will consider score transformation. Generalized estimating equations (GEE) with an exchangeable working correlation structure will be used to account for clustering within couples. Each model will also include an interaction term between treatment arm and gender to identify gender-specific effects. Given the small sample size and low power of homogeneity tests, if the p-value for the interaction term is ≥0.20, we will also report the

intervention effect for men and women combined (no interaction term). We will not be powered to detect other intervention effect modifiers unless gender is not a modifier, in which case we will explore modification by baseline values of the outcome being analyzed (e.g., is the intervention more effective at improving partner/family support among participants with low partner/family support at baseline), again using an interaction p-value <0.20 as our criteria for evidence of modification of the intervention effect. Finally, given the small sample size of this RCT, it is possible potential confounders remain imbalanced between treatment arms. We will repeat the above analyses (which already include gender), further including age and the baseline value of the outcome being analyzed, to adjust for residual confounding. The small sample, however, precludes from including additional covariates beyond these.

Objective 2: Primary analyses will follow an intent-to-treat protocol. We operationalize the outcomes in the negative (e.g., not retained, no active drug levels, no virologic suppression) such that the risk ratios (RR) for the intervention effect will be <1.0 if effective. We will estimate the intervention effect on dichotomous endpoints using separate *modified Poisson regression* models for each outcome to estimate risk ratios and 95% confidence intervals. Modified Poisson models use a robust standard error to estimate the RR with unbiased confidence intervals to avoid convergence problems with log linear models and to improve interpretation over logistic regression since the outcome is relatively common (>30%). If we still encounter problems with model convergence due to the small sample size, we will utilize logistic regression models instead. We will use GEE models with an interaction term between intervention arm and gender as described in Aim 1. We will also explore intervention effect modification and adjustment for other covariates as described in Aim 1.

Secondary analyses will also follow intent-to-treat protocol, again operationalizing the outcomes in the negative (monthly count of missed doses; monthly nonadherence) such that the rate or risk ratios will be <1.0 if the intervention is effective. We will estimate the intervention effect on the count of monthly missed doses using a negative binomial regression model to account for overdispersion due to an excessive amount of zero missed doses (perfect adherence). In addition to clustering of couples, each participant will have up to three observations (one for each month of follow-up). Participants LTFU will only contribute an observation for each completed month of follow-up for which there is a pill count, otherwise they are censored. Similarly, self-reported monthly nonadherence is likely to be heavily skewed with a large proportion of 0% nonadherence. As this is inherently a continuous measure (rather than a count), we will dichotomize as 0% nonadherence vs. >0% nonadherence and each participant will contribute an observation for each completed month of follow-up. A sensitivity analysis will be performed with dichotomization at ≤10% nonadherence vs. >10% nonadherence. As for the prior analyses, we will utilize GEE models (accounting for clustering of couples and repeated measures on individuals) with an interaction term between intervention arm and gender and will explore modification and adjustment for other covariates as described in Aim 1.

Objective 3: Following completed interviews, audio files will be transcribed by the interviewer, and the PI will code and analyze the interviews using MAXQDA 12® software. Framework Analysis will be used to identify responses to questions about the drivers, core facilitators, and barriers to intervention acceptability and success using grounded theory.[86] Two code maps will be developed to categorize data: (1) to understand the social, structural, and informational drivers, facilitators, barriers to recruiting, providing services for, and supporting discordant couples in

couple-based ANC and post-natal care; and (2) to understand concepts of “best-practice” for scaling up and implementing these services, particularly in regards to family engagement and using stories for educational purposes.

11. Ethical Considerations

The sites that participate in this proposal meet the requirements for the conduct of research using funds from the US Government. The protocol and consent forms will be reviewed and approved by the Vanderbilt University IRB (FWA00005756, IRB00000475-7, IRB00002125) and the Ministry of Health in Mozambique (FWA00003139 IRB# IRB00002657). The proposed project is Non-Exempt Human Subjects Research.

Recruitment and Consent of Serodiscordant Couples: Discordant couples who are identified during an ANC visit at one of the study sites will be asked a whether they would be willing to participate in a research study. If the couple is interested, they will be provided a consultation with the study assistant, at which point they will be asked to give informed consent through our consent form. This consent will include their willingness for us to access medical records and participate in survey sessions.

Recruitment and Consent of family members: Family members who agree to participate in the storytelling narrative sessions will be asked if they would be willing to participate in a research study. That study team member will describe the nature of the storytelling sessions and the possibility of their participation in a follow-up qualitative interview and ask if the person is interested in participating. If they are selected to participate in the interview, the study team member will organize a specific time/day for the interview. When the interviewer arrives, they will work with the provider to find a private room/space either at the home or within the community (whatever the preference of the participant).

Participant confidentiality

All participants who are consented in the study will be assigned a study ID number. Only study members will have the codebook that links the identifiers. Identifying information associated with these ID codes, such as names, will be kept in a data file separate from the survey data and clinic records. All data will be managed in a way that meets Vanderbilt IRB and Mozambique Bioethics standards for the protection of human subjects and to ensure confidentiality and the protection of sensitive health information.

A participant’s study information will not be released without the written permission of the participant. All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in locked rooms, i.e., access is limited to study staff. All study data collection, process, and administrative forms and other reports will be identified by a coded number to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator or informed consent forms, will be stored separately from study records identified by a code number. All databases will be secured with password-protected access systems. Forms, lists, logbooks, appointment books, and any other listings that

link participant ID numbers to other identifying information will be stored in a separate, locked file in an area with limited access.

Consent Procedures

The consent procedures are detailed above and the consent forms can be found in the Appendix (Appendices 5, 6, and 7). The signed consent forms will be kept in a lock box at the FGH office in Quelimane, separate from the transcripts of the interviews. The consent forms will be kept for seven years, at which point they will be burned to ensure that no one will be able to link any consents to participants.

Evaluation of benefits and risks

Adverse events

Risks to the subjects (both intervention and control group and family members): The level of risk associated with this research is expected to be minimal for all participants. Potential psychological discomfort may occur when administering the survey for participating couples, as many of the questions are personal and have to do with a stigmatized infectious disease. All participants are able to decline to answer any question that they deem uncomfortable.

Adverse Experience: We do not anticipate any adverse events as a result of this study, however study participants will be provided with a telephone number and instructed to contact study clinicians to report any serious AEs they experience.

Protection against risks: The study protocol and training manuals will include strict guidelines for conducting the survey and recording the data in a confidential manner. All study staff will receive formal responsible conduct of research training per NIH, VUMC, and Mozambican Ministry of Health guidelines. Participants may withdraw from the study for any reason at any time.

Benefits

For serodiscordant infected couples there is a possibility that storytelling engagement with family members will result in them gaining additional psychosocial support and education for their treatment. For these patients, they could experience improved health outcomes. The results of this evaluation may help us to offer better services for discordant couples who access services at the study clinics and throughout Mozambique. There could be a benefit to Mozambican society through improved health programs for people living with HIV.

12. Limitations

Our sample size of 35 couples in each arm is small, which limits our ability to detect a small change in behavior among couples. However, we believe this pilot will allow us to detect signals of an interventions success, which we can subsequently use to fund a larger trial.

13. Dissemination Plan

Results from this study will be collected into a report and will be shared with MISAU and the DPS. The results will also be disseminated to government officials and physicians working in these communities. If results are deemed by the authors to be potentially of interest to a wider scientific audience, we would plan on sharing these data in manuscript form, after obtaining appropriate clearances.

14. Budget

Description	TOTAL USD MZM		Study Details	
	USD	**MZ**	**Price per unit/ person (USD)**	**Number of people/ units**
Human Resources	**11,150**	**669,000**		
Project Officer	3,000	180,000	3,000	1 (20% effort)
Study Counselor	3,000	180,000	3,000	1
Interviewers for in-depth qualitative interviews	3,150	189,000	35	2(p)*45(d)
Storytelling implementer	2,000	120,000	2,000	1
TRAVEL & TRANSPORT	**1,130**	**67,800**		
maintenance for car/gas	900	54,000	45	20
bicycle repair kit	90	5,400	45	2
bicycle for storyteller	140	8,400	140	2
TRAINING/PROJECT ACTIVITIES	**9,045**	**542,700**		
Training for protocol implementation				
Per diem (food)	1,625	97,500	65	5(p)*5(d)
Venue hire (day)	500	30,000	100	5(d)
Training materials	1,000	60,000	1,000	1
Training for Storytellers supporters				
per diem (food)	1,300	78,000	65	10
Venue hire (day)	400	24,000	100	4
Training Materials	1,000	60,000	1,000	1
Supervision Activities				
Per diem (food)	1,820	109,200	65	4(d)*7(m)
Hiring of transport to/from site	1,400	84,000	100	14(d)
OTHER	**1,745**	**104,700**		

Photocopies of consent forms and questionnaire	500	30,000	0.25	2,000
basic nokia phone & credit for study counselor	195	11,700	15	13
Urine assay tests	1,050	63,000	5	210
Total of all costs	**23,070**	**1,384,200**		
Contingency 10%	**2,307**	**138,420**		
TOTAL	**25,377**	**1,522,620**		

15. Timeline

Month	Activities/Description
Month 1	Hire personnel & train them in PrEP specific protocols and delivery of Storytelling intervention
Month 2-7	Recruit of discordant couples in ANC
Months 2-9	Delivery of storytelling intervention to couples
Months 2-9	Collect quantitative survey data at baseline and 3 months
Months 5-9	Collect qualitative data from intervention couples
Month 7	Coding and data analysis of qualitative data
Month 9-10	Conduct quantitative data analysis of survey data and adherence measures
Month 11-12	Write up R01 grant to conduct a larger healer-initiated counseling and testing project.
Months 11-12	Disseminate findings via community meetings in Zambézia, to the Ministry of Health in Maputo, and PEPFAR partners.

16. Statement of Conflict of Interest

As the Principal Investigator, I will be responsible for the relevance and quality of the project research, and for the confidentiality and anonymity of the participants.

Statement of conflict of interests

I, Carolyn M. Audet, as Principal Investigator of the Project entitled "*Partners-based HIV Treatment for Sero-concordant Couples attending Antenatal Care: Increasing family-based support for PrEP adherence among discordant couples through storytelling*", declare that I am an employee of the Vanderbilt University Medical Center in Nashville, Tennessee, USA, working closely with Friends in Global Health (FGH) in Mozambique.

I am engaged in the interview and survey design process, the evaluation design approach, as well as in the production of the pilot intervention and evaluation protocol. I will also contribute in the analysis and presentation of the results of the above-mentioned evaluation, in collaboration with:

- VUMC's Institute of Global Health: non-profit entity committed to building capacity in low-resource settings through interdisciplinary global health educational and training programs, technical assistance to government and civil sector organizations, and implementation science and research in order to improve health and equity.
- FGH: wholly-owned subsidiary of VUMC, which supports HIV/ AIDS care and treatment programs (HIV adult and pediatric care and treatment, Prevention of Mother to Child Transmission (PMTCT), Counseling and Testing (CT) services, Tuberculosis (TB) program services and exposed child services (CCR) in 9 rural districts and the urban capital district within Zambézia Province.
- Provincial Health Directorate of Zambézia Province.

Finally, I would like to mention that the present pilot intervention and evaluation does not involve any personal financial benefits, nor is it a for-profit evaluation.

I declare that there are no conflicts of interest in the aforementioned Project:

Carolyn M. Audet

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18. Appendices

Appendix 1: List of Indicators/Data to Be Collected

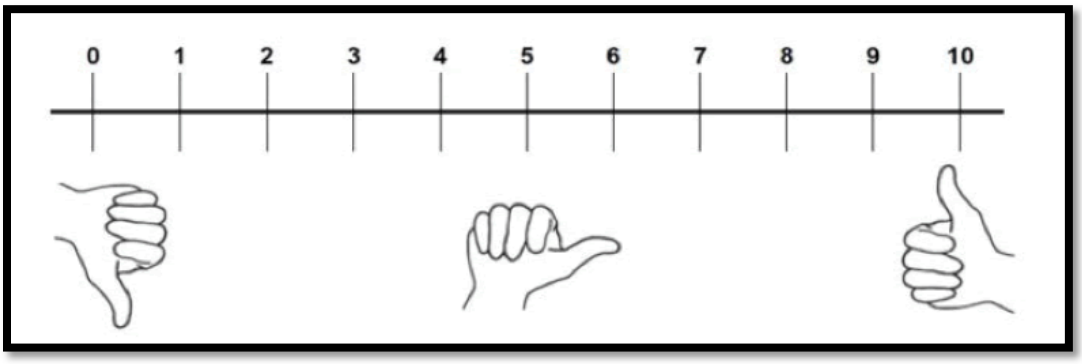
Demographics data (to be obtained from study registry documents and OpenMRS database)

1. Number of couples attending ANC
2. Number of couples eligible for study (female HIV-negative/ male HIV-positive)
3. Reasons for couples refusing entry into the study

4. District;
5. Health facility;
6. Urban (yes/no);
7. Main (*sede*) health facility (yes/no);
8. NID;
9. Sex;
10. Date of birth;
11. Age (years), at current enrollment;
12. Employment status at the time of enrollment;
13. Marital status of the patient at time of enrollment;
14. Sexual preference/orientation at time of enrollment;
15. Village, town, or city of residence at PrEP/ART initiation;
16. Previous ART enrollment (yes/no) (Male partner);
17. Previous ARV regimen before patient was LTFU (if applicable);
18. ART regimen at re-initiation/initiation (current medication regimen);
19. Enrollment date (current);
20. PrEP/ART initiation date (current);
21. WHO clinical stage at ART initiation, and date of documentation (male partner);
22. CD4+ cell count (cells/mm^3) 'at enrollment', taken between enrollment and 1 month after enrollment, and date of sample collection (male partner);
23. All CD4+ cell counts (cells/mm3) and dates of sample collections (male partner);
24. Viral load, first result obtained at or after enrollment, and results of any other VL tests, and date of sample collection (male partner);

25. All previous TB investigation results (positive/negative), and date of investigation (male partner);
26. Previous date of enrollment in TB services (if applicable) (male partner);
27. Previous TB treatment completed (yes/no) (if applicable) (male partner);
28. Previous date TB treatment completed (if applicable) (male partner);
29. Current enrollment in TB services, at (ART) enrollment, and date of documentation (male partner);
30. Weight (kg), at enrollment, and at all other clinic visits, and date of documentation;
31. Height (m^2), at enrollment, and date of documentation;
32. Body mass index (kg/m^2) at enrollment, and at all other clinic visits, and date of documentation;
33. Hemoglobin, at enrollment, and at all other clinic visits, and date of documentation;
34. Blood pressure, at enrollment, and at all other clinic visits, and date of documentation;
35. Alanine Transferase (ALT) at enrollment, at PrEP/ART initiation, and date of documentation;
36. Creatinine at enrollment, at ART initiation, and date of documentation;
37. Patient status (active, default, LTFU, transfer, or death) every month after enrollment;
38. Dates of all PrEP/ART pick-ups
39. Dates of all next scheduled PrEP/ART pick-ups;
40. Dates of all clinic visits
41. Dates of all next scheduled clinic visits;
42. Date cotrimoxazole (CTX) prescribed;
43. Patient reported use of intravenous (IV) drugs;
44. Patient reported use of tobacco;
45. Patient reported use of alcohol;
46. Estimated due date of pregnant female patient;
47. Initiation of any family planning method (Depo, pill, intrauterine device (IUD), implant, condoms, lactational amenorrhea [LAM], tubal ligation, vasectomy [male partner]), and date of initiation;
48. Continuation of any family planning method (Depo, pill, IUD, implant, condoms, LAM, tubal ligation), and date of continuation;
49. Final patient outcome status and date of final status:
    a. Transfer out of care at that facility, and date of transfer out;
    b. Death, date of death recorded, cause of death where available;
    c. LTFU, date of most recent visit (LTFU defined as not returning for >60 days past last scheduled appointment / pick-up date);

50. Number of babies with this pregnancy;
51. Concentration of PrEP in patient urine;
52. Monthly patient self-report of adherence using this scale:



(for each baby, if multiple live births this pregnancy)

53. Date of birth of infant(s);
54. Infant status at birth (alive, dead);
55. Sex of infant(s);
56. Weight of infant(s) at birth, and at all other clinic visits, and date of documentation;
57. Whether infant(s) received ART prophylaxis after birth, date of start, and type of ARV;
58. Data on infant feeding practices where available;
59. Date of any PCR testing for infant(s), and test results;
60. Date of any HIV rapid testing for infant(s), and test results;
61. Data on discharge from CCR services (transfers, referrals, abandoned, died), and date;
62. Health status of child(ren) at 18 months (alive, dead);
63. HIV health status of child(ren) at 18 months (HIV-positive, HIV-negative)

ANC-specific indicators (aggregated data, from OpenMRS and DHIS databases)

64. Number of pregnant women who arrived for first ANC appointment;
65. Number of pregnant women who know their serostatus, known positive;
66. Number of pregnant women who know their serostatus, recently tested;
67. Number of pregnant women who received HIV test results in ANC, first test (positive, negative, and indeterminate results);
68. Number of pregnant women who received HIV test results in ANC, repeat test, positive, negative, and indeterminate results);
69. Number of HIV-positive pregnant women enrolled in ANC;

70. Number of HIV-positive pregnant women who received ARVs to reduce risk of MTCT (NVP, AZT+NVP, initiated ART, and already on ART);
71. Number of pregnant women receiving CTZ upon entrance to ANC;
72. Number of HIV-positive pregnant women that initiate prophylaxis with CTZ;
73. Number of HIV-positive pregnant women who are clinically malnourished (DAM, DAG);
74. Number of HIV-positive pregnant women who receive nutritional support (supplemental and therapeutic);
75. Number of HIV-negative pregnant women who receive nutritional support (supplemental and therapeutic);
76. Number of pregnant women in ANC with HIV-negative results;
77. Number of partners of pregnant women present in ANC;
78. Number of partners of pregnant women who tested for HIV in ANC;
79. Number of partners of pregnant women who tested for HIV in ANC and received results, by test result (positive, negative, or indeterminate);
80. Number of HIV-positive partners of pregnant women who initiated ART in ANC.

Appendix 2: Storytelling Intervention

The three motivational stories include the following themes:

(1) A couple who has to overcome the difficulties associated with having a different HIV status compared to their partner. Specifically, how they address accusations of infidelity, how they manage to take different medications, interpret different messages (lifelong ART vs. short term PrEP), and a woman's concerns with seroconversion. How their family provides emotional and physical support via assistance in food preparation, completing chores around the house, and counseling both partners not to give up on the medication.

(2) A woman who overcomes the difficulties of an unsupportive husband and extended family. The story of a woman who wants to take PrEP but must take medication and attend clinical visits without detection. The challenges she encounters while hiding her treatment, the moment of discovery, and how she successfully changes the beliefs and attitudes of her husband and extended family.

(3) An encouraging couple who overcomes the difficulties of an unsupportive extended family. The story of a couple who support each other in medication adherence but face the scorn and derision of their extended family. The extended family blames the man for exposing the pregnant woman and her unborn child to HIV. The strategies this couple uses to change the attitudes and options of their family, to remain adherent to medication, and to have an HIV-uninfected baby.

Appendix 3: Measures used in study

1. Social Support (Berlin Social Support Scales)

Perceived Emotional Support

1. There are some people who truly like me.

2. Whenever I am not feeling well, other people show me that they are fond of me.

3. Whenever I am sad, there are people who cheer me up.

4. There is always someone there for me when I need comforting.

Perceived Instrumental Support

1. I know some people upon whom I can always rely.

2. When I am worried, there is someone who helps me.

3. There are people who offer me help when I need it.

4. When everything becomes too much for me to handle, others are there to help me.

Need for Support

1. When I am down, I need someone who boosts my spirits.

2. It is important for me always to have someone who listens to me.

3. Before making any important decisions, I absolutely need a second opinion.

4. I get along best without any outside help. (-)

Support Seeking

1. In critical situations, I prefer to ask others for their advice.

2. Whenever I am down, I look for someone to cheer me up again.

3. When I am worried, I reach out to someone to talk to.

4. If I do not know how to handle a situation, I ask others what they would do.

5. Whenever I need help, I ask for it.

<u>2. Relationship Empathy (Davis; Interpersonal Reactivity Index [IRI])</u>

1. I daydream and fantasize, with some regularity, about things that might happen to me.

2. I often have tender, concerned feelings for people less fortunate than me.

3. I sometimes find it difficult to see things from the "other guy's" point of view.

4. Sometimes I don't feel very sorry for other people when they are having problems.

5. I really get involved with the feelings of the characters in a novel.

6. In emergency situations, I feel apprehensive and ill-at-ease.

7. I am usually objective when I watch a movie or play, and I don't often get completely caught up in it.

8. I try to look at everybody's side of a disagreement before I make a decision.

9. When I see someone being taken advantage of, I feel kind of protective towards them.

10. I sometimes feel helpless when I am in the middle of a very emotional situation.

11. I sometimes try to understand my friends better by imagining how things look from their perspective.

12. Becoming extremely involved in a good book or movie is somewhat rare for me.

13. When I see someone get hurt, I tend to remain calm.

14. Other people's misfortunes do not usually disturb me a great deal.

15. If I'm sure I'm right about something, I don't waste much time listening to other people's arguments.

16. After seeing a play or movie, I have felt as though I were one of the characters.

17. Being in a tense emotional situation scares me.

18. When I see someone being treated unfairly, I sometimes don't feel very much pity for them.

19. I am usually pretty effective in dealing with emergencies.

20. I am often quite touched by things that I see happen.

21. I believe that there are two sides to every question and try to look at them both.

22. I would describe myself as a pretty soft-hearted person.

23. When I watch a good movie, I can very easily put myself in the place of a leading character.

24. I tend to lose control during emergencies.

25. When I'm upset at someone, I usually try to "put myself in his shoes" for a while.

26. When I am reading an interesting story or novel, I imagine how I would feel if the events in the story were happening to me.

27. When I see someone who badly needs help in an emergency, I go to pieces.

28. Before criticizing somebody, I try to imagine how I would feel if I were in their place.

3. Patient Health Questionnaire - 9 (PHQ-9 Depression Screening tool)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

1. Little interest or pleasure in doing things.

2. Feeling down, depressed, or hopeless.

3. Trouble falling or staying asleep or sleeping too much.

4. Feeling tired or having little energy.

5. Poor appetite or overeating.

6. Feeling bad about yourself - or that you are a failure or have let yourself or your family down.

7. Trouble concentrating on things, such as reading the newspaper or watching television.

8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.

9. Thoughts that you would be better off dead or of hurting yourself in some way.

4. Relationship Satisfaction:

1. How well does your partner meet your needs?
2. In general, how satisfied are you with your relationship?
3. How good is your relationship compared to most?
4. How often do you wish you hadn't gotten into this relationship?
5. To what extent has your relationship met your original expectations?
6. How much do you love your partner?
7. How many problems are there in your relationship?

5. Self-Efficacy Beliefs

"I believe that I can ….

1. Keep a clinic appointment
2. Follow overall treatment regimen
3. Follow a plan for taking PrEP medication
4. Take my PrEP Medication with correct intervals
5. Take correct dose of my medications
6. take my medications while I am at the farm
7. Take my medications on a weekday
8. Take my medications on a weekend
9. Take my medications if I am travelling
10. Take my medications even if I feel well
11. Take my medications even if I feel ill
12. Take my medications even if I am having medication side effects
13. Take my medications even if I am having a personal crisis

6. Outcome Expectancy

If I take my PrEP medication regularly I will….

1. be healthy
2. have a good quality of life
3. have a long life
4. lead a normal life
5. avoid getting HIV

Appendix 4: Semi-structured interview guide for intervention couples and their families

***Note**: For use in completing in-depth interviews with couples and with their families.*

Intervention Couple questions

1. Tell me what were the common messages your heard in the PrEP stories? Did they sound like issues that might be common here in Zambézia?
2. Did you think the stories addressed the major concerns people have with PrEP during pregnancy here in Mozambique? What did they miss?
3. What were your favorite parts of the stories? What parts did you like the least?
4. How have the stories impacted your motivation to take your medication? (what is the most important reason you take your medications? If you don't take them, why are you not motivated?)
5. How did the story impact your belief in your ability to take the medication every day? (what strategies did you learn that help you remember to take your medications?)
6. If you take your medications regularly, do you believe you can remain HIV-uninfected?
7. Did the stories change your partners view about taking medications?
8. Did the stories change your family's attitudes towards discordant couples staying together? Did the stories change your family's view of PrEP/ART use?

Intervention Family questions

1. Tell me what were the messages your heard in the PrEP stories? Did they sound like issues that might be common here in Zambézia?
2. Did you think the stories addressed the major concerns people have with PrEP during pregnancy here in Mozambique? What did they miss?
3. What were your favorite parts of the stories? What parts did you like the least?
4. Do you think that an HIV-negative pregnant woman should stay with an HIV-positive man? Should she continue to have sex with him?
5. Did the stories change your view of PrEP?
6. Did the stories change your view of discordant couples?
7. How did hearing the stories help you provide support to your family? (things to say, ways to help?)
8. Do you believe that PrEP can prevent a pregnant woman from contracting HIV? What are some reasons it might not work?
9. If you were making up your own stories to help discordant couples and their families, what are other topics you would add? What else would be helpful to know?

Appendix 5: Informed Consent Form for participant (intervention arm)

KEY ELEMENTS OF THE STUDY

1. This consent form contains information about a new study to provide a storytelling intervention to serodiscordant expectant couples.

2. Couples who are in the intervention group of this study will have the opportunity to listen to three stories that will educate and help support them to stay adherent to their medication, and will complete two interview surveys.

3. Couples in the control group will complete two interview surveys, but otherwise will enroll in PrEP and HIV care and treatment as they would normally.

4. You have been selected to receive three storytelling sessions, along with any family members you want to include.

5. If you agree to participate in the study, a study staff person will conduct a survey now and again at six months after you start medication.

6. You can stop participating in the study at any time without penalty.

This informed consent document applies to adults 18 years or older. This document is to be read aloud to the participants in the intervention arm.

Age of participant: _____

Introduction

This consent form contains information about a new study to provide couples-based PrEP medication that will help prevent someone being infected with HIV and HIV care and treatment for discordant pregnant couples.

You have been selected because you attended antenatal care visit and tested HIV-negative while your partner is HIV-positive (serodiscordant couples) and you are 18 years or older.

This form describes your rights as a participant. It is meant to answer your questions. We will read this form to you. Please feel free to ask any questions you may have about this.

If you and your partner agree to participate in this program I will ask you to sign the form or make your thumbprint mark. Even if you agree to participate, you can stop participating at any time. I will give you a copy of this form. This form might contain some words that are unfamiliar to you. Please ask me to explain anything you do not understand.

Purpose of this study

This study is being done by staff from Vanderbilt University Medical Center (VUMC) and Friends in Global Health (FGH). We want to try a new way to offer PrEP and HIV care and treatment to couples where one person is HIV-positive and the other HIV-negative who are expecting a child. Right now, couples can receive PrEP and HIV care together in HIV treatment services, but their counseling and education is limited to short education sessions and does not engage their families.

Couples who are in the intervention group of this study will have the opportunity to listen to three stories that will educate and help support them to stay adherent to their medication. Couples in the control group will complete two surveys, but otherwise will enroll in PrEP and HIV care and treatment as they would normally. We want to see if couples who get the additional storytelling sessions are better at staying on treatment compared to couples in regular care.

Procedures to be followed and approximate duration of the study

You have been selected to receive the storytelling sessions.

This study will begin today and last for the next 6 months. If you and your partner agree to be part of this study, we will enroll you both into PrEP / HIV care and treatment. All future clinical visits, drugs, and tests to assess medication levels in your body will be given to you at the ANC or CCR clinics.

Our study assistant will arrange a meeting with you and the storytellers in the next two weeks. Your storyteller will arrange three times to come to the family home (or a location of your choice) to tell each story to you and to any family members that you would be willing to disclose your treatment to. We will access your and your baby's medical records to see what medications you are taking, medical data about your health (drug levels, CD4 cell count and viral load), and the dates you pick up your medications.

A study staff person will also conduct two surveys at the beginning of your treatment and at six months after you start treatment. You do not need to answer all the questions in the surveys if you do not want to. If a question makes you feel uncomfortable or you do not know the answer, it is ok to tell the interviewer that you do not want to answer the question. You can also stop the surveys at any time without any penalty.

Some couples enrolled in the study will be asked to participate in an interview to describe their experience with the program and costs related to your and your family's health care. This interview will occur at least 6 months after enrollment. You do not need to answer the questions if you do not want to. If a question makes you feel uncomfortable or you do not know the answer, it is ok to tell the interviewer that you do not want to answer the question. You can also stop the interview at any time without penalty.

Expected Costs:

None.

Possible Risks

The idea of providing stories to education and motivate discordant couples (and their families) expecting a baby is new and untested. While we will provide support, there is a chance that you and your partner will not agree on ways to take medication or talk together. This could make more problems in your relationship. If you feel any discomfort or have relationship problems, please contact us as soon as possible so we can work to resolve it together.

We know that talking about your personal experiences with HIV with your partner or health care workers can be uncomfortable. We will try to have a comfortable, honest, and relaxed discussion. Still we know that some of the questions we ask might make you feel uncomfortable. We will try to limit embarrassment as much as possible. No study staff will tell anyone else your responses to the survey questions.

Possible Benefits

The information you share may help us to offer better services for serodiscordant couples who come for ANC services. This could benefit Mozambican society by improving health programs for people living with HIV. If the project is successful, you may have better communication and trust with your partner after our counseling sessions.

What happens if you choose to withdraw from study participation?

Nothing. You are free to stop participating at any point without problem. You only need to say that you would like to stop being in the study. You can tell this to us at any time.

Confidentiality

We will make every effort to keep your personal information confidential. However, it is not possible to guarantee total confidentiality. The clinical information obtained during this study will be kept with your medical record and stored securely at the health facility in locked areas and on a protected database. Only trained medical and study staff will have to access this clinical information.

The information related to the study activities will be kept at the health facility and at FGH offices in locked secure areas. Only trained study staff will have access to this study information.

Privacy Information

Your information may only be shared if you or someone else is in danger, or if we are required to do so by law. If this occurs, your information may be shared with VUMC, or the U.S. and/or Mozambican government. This includes, for example, the VUMC IRB, U.S. Federal Government Office for Human Research Protections, or the Mozambican Ministry of Health.

Contact Information for Questions

If you should have any questions about study or wish to have additional counseling related to your care, please feel free to contact the HoPS+ study manager, Almiro Emilio, at the FGH office in Quelimane at +258 24217593.

For more information about giving consent or your rights, please feel free to contact the National Committee for Bioethics of Health in Mozambique at +258 824066350. You may also contact the

VUMC Institutional Review Board (IRB) office in the U.S. at +001-615-322-2918 or toll free at +001-866-224-8273.

Do you have any questions?

This form has been read and explained to me. I have been given an opportunity to ask questions I have about the study. I understand that I may decide at any time that I do not want to continue participating in the study. I understand that I will receive a copy of this consent form. By saying yes, you agree to participate in the study for 6 months. You are agreeing to participate in our interviewer-administered surveys and that we can look at your medical records, and that of your unborn child. By saying no, you decline to participate in all parts of the study.

Moderator: Answer the participant's questions before proceeding to the next question.

I give my consent to participate in the study. ☐ Female partner ☐ Male Partner

_____ _____

Printed Name of Participant Date

_____ _____

Signature of Participant Date

Thumbprint of Participant

_____ _____

Signature of Witness (if thumbprint used) Date

_____ _____

Signature of Person Who Explained This Form Date

I have explained to the participant the study purpose and procedures and we have discussed all the risks that are involved. I have answered questions to the best of my ability.

Appendix 6: Informed Consent Form for participant (control arm)

This informed consent document applies to adults 18 years or older. This document is to be read aloud to the participants in the control arm.

KEY ELEMENTS

1. This consent form contains information about a new study to provide a storytelling intervention to serodiscordant expectant couples.

2. Couples who are in the intervention group of this study will have the opportunity to listen to three stories that will educate and help support them to stay adherent to their medication, and will complete two interview surveys.

3. Couples in the control group will complete two interview surveys, but otherwise will enroll in PrEP and HIV care and treatment as they would normally.

4. You have been selected for the control group. This means you will get all the clinical care that you usually would get at this health facility.

5. If you agree to participate in the study, a study staff person will conduct a survey now and again at six months after you start medication.

6. You can stop participating in the study at any time without penalty.

Age of participant: _____

Introduction

This consent form contains information about a new study to provide a storytelling intervention to serodiscordant pregnant couples. This form describes your rights as a participant. It is meant to answer your questions. We will read this form to you. Please feel free to ask any questions you may have about this.

You have been selected because you attended antenatal care visit and tested HIV-negative while your partner is HIV-positive (serodiscordant couples) and you are 18 years or older.

If you and your partner agree to participate in this program, I will ask you to sign the form or make your thumbprint mark. Even if you agree to participate, you can stop participating at any time. I will give you a copy of this form. This form might contain some words that are unfamiliar to you. Please ask me to explain anything you do not understand.

Purpose of this study

This study is being done by staff from Vanderbilt University Medical Center (VUMC) and Friends in Global Health (FGH). We want to try a new way to offer PrEP and HIV care and treatment to

couples where one person is HIV-positive and the other HIV-negative who are expecting a child. Right now, couples can receive PrEP and HIV care together in HIV treatment services, but their counseling and education is limited to short education sessions and does not engage their families.

Couples who are in the intervention group of this study will have the opportunity to listen to three stories that will educate and help support them to stay adherent to their medication. Couples in the control group will complete two surveys, but otherwise will enroll in PrEP and HIV care and treatment as they would normally. We want to see if couples who get the additional storytelling sessions are better at staying on treatment compared to couples in regular care.

Procedures to be followed and approximate duration of the study

You have been selected for the control group. This means you will get all the clinical care that you usually would get at this health facility.

This study will begin today and last for the next year. If you and your partner agree to be part of this study, you will enroll into PrEP and HIV care and treatment today. All future clinical visits, drug pick-ups, and tests to assess medication levels in your body will be given to you at the ANC or CCR clinics. After you are enrolled on medication, you and your partner will be brought to meet with the study assistant who will ask you and your partner to complete a survey.

A study staff person will also conduct the same survey at six months after you start treatment. If you give us permission, we can complete this survey at the health facility or at your home (depending on your preference). You do not need to answer all the questions in the surveys if you do not want to. If a question makes you feel uncomfortable or you do not know the answer, it is ok to tell the Interviewer that you do not want to answer the question. You can also stop the surveys at any time without any penalty.

Expected Costs:

None

Possible Risks

We know that talking about your personal experiences with HIV with your partner or health care workers can be uncomfortable. We will try to have a comfortable, honest, and relaxed discussion. Still we know that some of the questions we ask might make you feel uncomfortable. We will try to limit embarrassment as much as possible. No study staff will tell anyone else your responses to the survey questions.

Possible Benefits

The information you share may help us to offer better services for serodiscordant couples who come for ANC services. This could benefit Mozambican society by improving health programs for discordant people expecting a child. If the project is successful, you may have better communication and trust with your partner after our storytelling sessions.

What happens if you choose to withdraw from study participation?

Nothing. You are free to stop participating at any point without problem. You only need to say that you would like to stop being in the study. You can tell this to us at any time.

Confidentiality

We will make every effort to keep your personal information confidential. However, it is not possible to guarantee total confidentiality. The clinical information obtained during this study will be kept with your medical record and stored securely at the health facility in locked areas and on a protected database. Only trained medical and study staff will have access to this clinical information.

The information related to the study activities will be kept at the health facility and at FGH offices in locked secure areas. Only trained study staff will have access to this study information.

Privacy Information

Your information may only be shared if you or someone else is in danger, or if we are required to do so by law. If this occurs, your information may be shared with VUMC, or the U.S. and/or Mozambican government. This includes, for example, the VUMC IRB, U.S. Federal Government Office for Human Research Protections, or the Mozambican Ministry of Health.

Contact Information for Questions

If you should have any questions about this study or wish to have additional counseling related to your care, please feel free to contact the HoPS+ study manager, Almiro Emilio, at the FGH office in Quelimane at +258 24217593 or toll free at +001-866-224-8273.

For more information about giving consent or your rights, please feel free to contact the National Committee for Bioethics of Health in Mozambique at +258 824066350. You may also contact the VUMC Institutional Review Board (IRB) office in the U.S. at +001-615-322-2918.

Do you have any questions?

This form has been read and explained to you. You have been given an opportunity to ask questions about the study. You know that you may decide at any time to not continue participating in the study. You understand that you will receive a copy of this consent form. By saying yes, you agree to participate in two surveys: one now and another in six months. You are agreeing that we can look at your medical records, and that of your unborn child. If you say no, you decline to participate in all parts of the study.

Moderator: Answer the participant's questions before proceeding to the next question.

I give my consent to participate in the study. ☐ Female partner ☐ Male Partner

_____ _____

Printed Name of Participant Date

_____	_____	Thumbprint of Participant
Signature of Participant	Date	
_____	_____	
Signature of Witness (if thumbprint used)	Date	
_____	_____	
Signature of Person Who Explained This Form	Date	

I have explained to the participant the study purpose and procedures and we have discussed all the risks that are involved. I have answered questions to the best of my ability.

Appendix 7: Informed Consent Form for Family Member Interview

This informed consent document applies to adults 18 years or older. This document is to be read aloud to the participants.

KEY ELEMENTS

1. This consent form contains information about a new study to provide a storytelling intervention to serodiscordant expectant couples.

2. Couples who are in the intervention group of this study will have the opportunity to listen to three stories that will educate and help support them to stay adherent to their medication, and will complete two interview surveys.

3. Family members of those in the intervention group are also invited to listen to the stories.

4. You are invited to listen to three storytelling sessions to help you learn more about PrEP and about ways you can support your family.

5. If you agree to participate in the study, a study staff person may request to conduct a single interview with you 4-6 months from now.

6. You can stop participating in the study at any time without penalty.

Age of participant: _____

Introduction

This consent form contains information for family members who participate in a storytelling intervention with discordant couples expecting a child.

You have been selected because you were nominated by a family member to participate in the story-telling study.

This form describes your rights as a participant. It is meant to answer your questions. We will read this form to you. Please feel free to ask any questions you may have about this.

If you agree to participate in this project I will ask you to sign the form. Even if you agree to participate, you can stop participating at any time. I will give you a copy of this form if you would like one. This form might contain some words that are unfamiliar to you. Please ask me to explain anything you do not understand.

Purpose of this study

This study is being done by staff from Vanderbilt University Medical Center (VUMC) and Friends in Global Health (FGH), in collaboration with the Provincial health authorities, as a part of the PrEP storytelling study. In the storytelling study we want to try a new way to educate and motivate discordant couples who are expecting a child to adhere to their medication. In conducting this project, we want to include you in this study and investigate your perspectives and experiences listening to the stories, supporting your discordant family member in taking their medications, and any suggestions you may have for program implementation and improvement.

Procedures to be followed and approximate duration of the interview

Participants who are nominated to listen to stories with their families will have the opportunity to listen to 3 stories about the importance of PrEP, some challenges to taking PrEP, and ways we can help friends and family members take their medication. The stories will be delivered at the home, or in the preferred location, of the couple who nominated you. You can come to listen to any of the stories that you wish.

Some family members will be asked to complete an interview. If you are selected, the interview will last an estimated 30-45 minutes. If you agree to participate in this interview, a study staff person will conduct the interview with you now, or at a scheduled time in the near future of your choosing.

You do not need to answer all the questions in the interview if you do not want to. If a question makes you feel uncomfortable or you do not know the answer, it is ok to tell the interviewer that you do not want to answer the question. You can also stop the interview at any time without any penalty.

Your responses to this interview will be recorded in an audio recording. The recording will be kept on a secure audio file at the FGH office in Quelimane. The recording will be transcribed (copied) into a written document. We will use this transcribed data to do data analysis at the end of this study. Before we use this data all of your identifying information will be taken out. It will not be possible for anyone to know it is your responses or information. The transcriptions will be kept and securely stored on password-protected servers and computers of study personnel at the FGH office in Quelimane, and principal investigator at VUMC. After 6 years the transcript files will be destroyed (as suggested by VUMC IRB).

Expected Costs:

None.

Possible Risks

Listening to stories about discordant couples may be challenging, given that you are close with the couple who nominated you. It may make you feel sad when you think of the challenges they face. If you are selected to participate in the interview, we do not anticipate any possible risks with participating in this interview. We will try to have a comfortable, honest, and relaxed discussion. We will try to limit any discomfort as much as possible. If you feel any

discomfort, please contact us as soon as possible so we can work to resolve it together. No study staff will tell anyone else your responses to the interview questions.

Possible Benefits

You may learn a great deal about PrEP and how people can keep themselves from contracting HIV if you attend the storytelling sessions. If you are selected to participate in an interview, the information you share may help us to offer better services for serodiscordant couples who seek ANC services, and for families affected by HIV. This could benefit Mozambican society by improving health programs for people at risk of HIV acquisition.

What happens if you choose to withdraw from interview participation?

Nothing. You are free to stop participating at any point without problem. If you want to stop attending the stories, you can simple stop attending. If we are conducting the interview and you want to stop, you only need to say that you would like to stop being in the interview. You can tell this to us at any time.

Confidentiality

If you are selected to participate in the interview we will make every effort to keep your responses confidential. However, it's not possible to guarantee total confidentiality. The information obtained during this interview will be kept with the trained study team, stored securely in the FGH office in Quelimane and with the principal investigator at VUMC.

Privacy Information

Your information may only be shared if you or someone else is in danger, or if we are required to do so by law. If this occurs, your information may be shared with VUMC, or the U.S. and/or Mozambican government. This includes, for example, the VUMC IRB, U.S. Federal Government Office for Human Research Protections, or the Mozambican Ministry of Health.

Contact Information for Questions

If you should have any questions about this study, please feel free to contact the HoPS+ study manager, Almiro Emilio, at the FGH office in Quelimane at +258 24217593.

For more information about giving consent or your rights, please feel free to contact the National Committee for Bioethics of Health in Mozambique at +258 824066350. You may also contact the VUMC Institutional Review Board (IRB) office in the U.S. at +001-615-322-2918 or toll free at +001-866-224-8273.

Do you have any questions?

This form has been read and explained to you. You have been given an opportunity to ask questions you have about the interview. You understand that you may decide at any time that you do not want to continue participating in the interview. You understand that you can receive

a copy of this consent form. By saying yes, you agree to participate in this study. By saying no, you decline to participate in the study.

Moderator: Answer the participant's questions before proceeding to the next question.

I give my consent to participate in the interview.

Relationship with Couple _____

_____ _____

Printed Name of Participant Date

Thumbprint of Participant

_____

Signature of Participant Date

_____ _____

Signature of Person Who Explained This Form Date

I have explained to the participant the purpose of the study and procedures and we have discussed all the risks that are involved. I have answered questions to the best of my ability.