Study Protocol

Protocol Title:
Postpartum HIV care engagement in the context of Option B+ in Tanzania

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Version
July 23, 2018

1. Research Design

Background

The goal of this study is to examine the implementation of the Option B+ protocol, whereby all HIV-infected pregnant women initiate lifelong antiretroviral therapy (ART) during pregnancy, regardless of CD4 count or clinical staging. The Option B+ approach of establishing lifelong ART for pregnant women holds great promise for improving women's long-term health and moving towards an "AIDS free generation."[1] At the same time, there have been concerns about implementation challenges, particularly with retention and adherence in the postpartum period.[2,3] Data from multiple African settings suggest that one-third to one-half of all women who start ART during pregnancy are lost to care within six months after childbirth.[4-8] Retention in care and sustained adherence to ART following childbirth are vital to the success of the Option B+ protocol, to ensure the viral suppression of the woman, to prevent HIV transmission to her child during breastfeeding, and to reduce the probability that she might transmit HIV to her sexual partners.[9]

This study is filling a critical void in understanding the implementation of Option B+, and will identify opportunities to strengthen programmatic efforts to support women's long-term care engagement. Using the Consolidated Framework for Implementation Research, this study examines the Option B+ protocol in the sites in Tanzania, seeking multiple perspectives (facilities, providers, patients) and using multiple methods (observations, surveys, record reviews, qualitative interviews/ discussions). Taken together, these data can help to identify bottlenecks and barriers, and inform interventions to promote women's care engagement and optimal medication adherence in the postpartum period. Preliminary findings from our cohort demonstrate the need to address stigma among pregnant women navigating PMTCT services. Therefore, this study will also develop and pilot test an intervention that addresses stigma at early entry into PMTCT.

Study aims

This study is addressing four specific aims:

Aim #1: Examine the facility-level implementation of Option B+ in several diverse care delivery sites in the Kilimanjaro region, focusing on women's HIV care engagement in the postpartum period. *Methods*: At sites within the Moshi Urban and Moshi Rural districts of the Kilimanjaro Region, we will document practices to support postpartum HIV care engagement through clinical observations; explore implementation processes and barriers through key informant interviews with health care providers (n=30); and examine retention in care outcomes through medical record reviews of all pregnant women receiving ART through the B+ protocol since the policy was implemented in February 2014 (n=512).

Aim #2: Examine patient-level factors that impede or support postpartum care engagement among women initiating or continuing ART during pregnancy. *Methods*: Over a six-month period, we will enroll up to 200 women who are HIV-infected and either initiating or continuing ART during pregnancy at sites in the same clinic sites described in Aim #1, which lie in the Moshi Rural and Moshi Urban districts of the Kilimanjaro Region. We will conduct baseline surveys in the second or third trimester of pregnancy, and follow-up surveys at 3 and 6 months postpartum. We will retain participants' contact information and may contact them for additional surveys up to 24 months postpartum. Surveys will measure potential predictors (intrapersonal, interpersonal and facility issues) that affect engagement in HIV care (ART receipt and adherence) in the postpartum period. For participants who have not had viral load testing as part of their standard of care, we will also test for viral load at 6 months postpartum as a marker of ART adherence, with drug resistant resistance testing if the viral load test yields a result of greater than 1000 copies/ml. We will access participants' medical records during the study period to abstract clinical data and capture it in a de-identified database. We began enrollment in our cohort on 19 July 2016, and completed our enrollment of 200 women on 7 August 2017. Women were enrolled across nine sites in the Moshi Urban and Moshi Rural areas (Majengo, Pasua, KCMC, St. Joseph's, Bondeni, Msaranga, Himo, Faraja, and Cogi Health Centres). A subset of women (n=24) completed in-depth interviews during pregnancy and again in the postpartum period, to examine the complex interplay of individual, social and contextual factors that influence HIV care for women following childbirth.

Aim #3: Identify opportunities to improve implementation of Option B+ so that it enhances and promotes continuous care in HIV services following childbirth, including the development of a brief, theory-based intervention and methodological protocol to address HIV stigma at entry into ANC. *Methods*: We will conduct focus group discussions (FGDs) and in-depth interviews at the same clinic sites described in Aim #2, with the following populations: health care providers (n=5 IDIs or FGDs; including HIV care providers, PMTCT coordinators, and ANC nurses); home-based HIV care workers (n=16; 2 FGDs); HIV-infected pregnant and postpartum women (n=18 IDIs); and HIV-uninfected pregnant and postpartum women (n=12 IDIs). These discussions will identify opportunities to improve implementation of the national PMTCT policy to support continuous care engagement in the postpartum period and will inform the content and protocol of the *Maisha* intervention. Intervention ideas will be further discussed and refined through a community stakeholder meeting. We will also conduct ~40 observation hours in each of the two clinic sites (Majengo and Pasua) selected for the pilot trial and record detailed notes on clinic flow and opportunities to integrate study activities into routine care. We will conduct cognitive interviews with 10 HIV-infected women to revise our study surveys and assess whether our stigma measures capture the intended constructs. We will also conduct a trial run of the full *Maisha* intervention with HIV-infected pregnant/postpartum women (n=6) to refine and finalize the intervention curriculum and study protocol.

Aim #4: Conduct a pilot randomized controlled trial (RCT) of *Maisha* to examine 1) feasibility and acceptability in an ANC setting, and 2) impact on early retention in PMTCT, HIV disclosure, and constructs of HIV stigma. *Methods:* We will conduct a pilot RCT with 150 women, both HIV-infected (n=25 *Maisha*; 25 Standard of Care, SoC) and HIV-uninfected (n=50 *Maisha*; 50 SoC. Women will be randomized to receive either the SoC HIV testing and counseling, or SoC plus the *Maisha* intervention. Participants will complete a baseline survey and a follow-up survey at 3 months. Surveys will include measures for health outcomes (e.g., HIV care engagement, adherence to ART, depression, HIV testing), stigma outcomes (e.g., anticipated stigma, enacted stigma, internalized stigma), and other secondary outcomes or potential covariates (e.g., partner support, attitudes to ART, intimate partner violence). A subset of 15 HIV-infected intervention patients will participate in a qualitative in-depth interview at 3 months to provide feedback on the intervention. Clinical data will be abstracted from the medical records of participants completing the 3-month survey.

Overview and timeline

This 5-year study (2016-2021) seeks to understand and inform the implementation of the Option B+ protocol for PMTCT care in the Kilimanjaro Region of Tanzania, and develop an intervention to support women who are newly pregnant and being tested for HIV. The work is being completed in diverse clinical settings, using a multi-methods approach informed by the Consolidated Framework for Implementation Research (Table 1).

Table 1: Study timeline

AIMS	METHODS	YEAR 1				YEAR 2				YEAR 3				YEAR 4				YEAR 5			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Aim 1: Examine implementation of B+ for postpartum care engagement	Observations to assess services and fidelity to protocol																				
	Key informant interviews to assess process and barriers																				
	Record review to assess care engagement outcomes (n=512)																				
Aim 2: Identify factors that impact postpartum care engagement	Enroll pregnant women on ART at clinic sites (n=200)																				
	Follow-up interviews at 3m and 6m postpartum with possible additional surveys up to 2 years post-partum																				
	In-depth interviews to explore care engagement process (n=24)																				
Aim 3: Identify opportunities to promote postpartum care engagement under B+	Stakeholder feedback meeting & dissemination																				
	Focus group discussions and in-depth interviews with stakeholders at each site																				
	Conduct clinic interviews & observations; refine measures																				
	Analyze data, prepare draft curriculum & record video																				
	Trial run; feedback from advisory board & FGDs; refine & revise																				
Aim 4: Pilot test	Finalize the pilot study protocol																				
	Recruit, baseline & deliver intervention vs. SoC																				
	Conduct 3-month follow up with participants (n=50 HIV+ & 100 HIV-)																				
	Analyze data, write manuscripts & prepare R01																				

Setting

The research will be conducted in diverse clinical sites in the Moshi region that provide PMTCT services. Those sites will be identified in consultation with the Ministry of Health, considering both patient load and capacity to absorb research.

Study procedures by phase

Phase 1: Observations and key informant interviews

First, the KCMC team and the Duke graduate student will conduct *semi-structured observations* in relevant clinical areas in order to document the process of implementing the national PMTCT protocol to promote postpartum HIV care engagement. Observations will include a review of protocols, practices and record keeping procedures. Observations will focus on the services specifically meant to promote engagement in HIV care for women in the postpartum period (e.g., counseling across the perinatal continuum, monitoring of patient retention, transfer of care from antenatal care to reproductive & child health to HIV care & treatment). Following informed

consent specific to clinic observation, the observations will be conducted by a KCMC staff member and the Duke graduate student, who will spend approximately 5 weeks conducting observations on clinic days, using a combination of checklists and ethnographic observation tools.

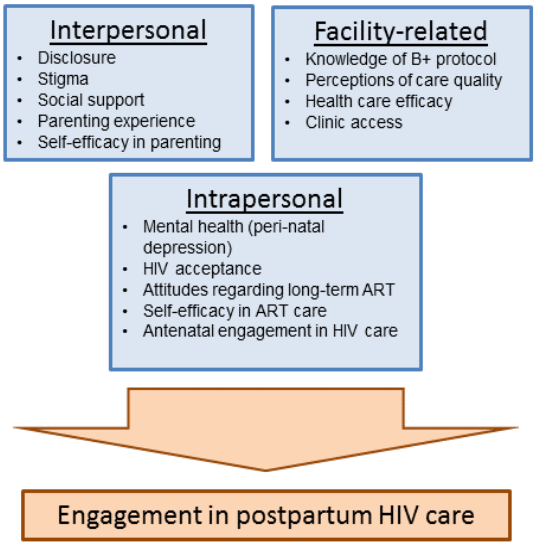
Second, the KCMC team and the Duke graduate student will conduct *key informant interviews with health care providers*, in order to understand the implementation process and barriers. The following stakeholders will be interviewed (distributed evenly across sites): attending physicians (n=3), ANC nurses (n=6), RCH nurses (n=6), counselors (n=6), community health workers (n=6), and managers (n=3). Interviews will be conducted by a KCMC staff member and the Duke graduate student, with semi-structured guides developed for each distinct stakeholder group. Interviews will focus on issues related to perceptions of policy guidelines, experience with implementing guidelines, work environment and burden, training and perceived capacity, and perceptions of bottlenecks/barriers to postpartum care engagement. Interviews will be conducted after the observations in order to cross-check and provide greater context for the observational data. Following informed consent, the KCMC research nurse and the Duke graduate student will conduct the interviews in Kiswahili or English (depending on participant's preference), using a semi-structured guide. Interviews will be audio-recorded with participants' permission. Interviews will last approximately 60 minutes.

Phase 2: Surveys and In-depth Interviews with female patients

Procedure: Over a twelve-month period, we will enroll women (n=200) who are HIV-infected and either initiating or continuing ART during pregnancy at sites in the Kilimanjaro region. We will conduct baseline surveys in the second or third trimester of pregnancy, and follow-up surveys at 3 and 6 months postpartum. We will also contact participants shortly after the birth of their child to complete a brief research form to obtain information about the birth and any changes in the participant's engagement in care. Additionally, in the event of the child's death, we will contact participants 4-6 weeks after the loss to complete a brief research form and obtain information about what occurred. Participant contact information will be retained and we may contact participants for additional surveys at critical time points in their care (i.e., transition of HIV care from the ANC back to CTC facility) for up to 2 years postpartum. Surveys will measure potential predictors (intrapersonal, interpersonal and facility issues, including transferring between clinics for care) that affect engagement in HIV care (ART receipt and adherence) in the postpartum period. De-identified clinical data will be abstracted from participants' medical records during the study period, up to two years postpartum. A subset of women (n=24) will complete in-depth interviews during their third trimester and again during the postpartum period, to examine the complex interplay of individual, social and contextual factors that influence HIV care for women following childbirth. Participants will complete an interviewer-administered structured survey, conducted by a research nurse at a minimum of three time points, with the potential to add additional time points as resources allow. For participants who have not received viral load testing as part of their standard of care, blood will be collected at 6 months postpartum by the research nurse for viral load testing. If the participant's viral load is measured at greater than 1000 copies/ml, follow-up testing will be conducted to test for drug resistance.

- *Pregnancy*: Complete the baseline assessment in the second or third trimester of pregnancy, with a target date of 30 weeks gestation.
- *Birth:* Complete brief research form approximately 1-2 weeks after delivery.
- *3 months postpartum*: Complete the second survey at approximately 3 months after the birth of the child.
- *6 months postpartum*: Complete the second survey at approximately 6 months after the birth of the child. Blood samples for viral load testing will also be collected at this time point.
- *Up to 2 years postpartum*: As study resources allow, we will contact participants up to 24 months postpartum to repeat the survey measure.
- *Death of child:* In the event of the death of the child, complete brief research form.

Figure 2: Conceptual model guiding cohort measures



Patient-level data will be collected for the purpose of identifying factors that should be addressed in implementation. All assessments will include questions about demographics and key constructs reflecting intrapersonal issues (e.g., mental health and self-efficacy for ART care), interpersonal issues (e.g., disclosure and social support), and facility-related issues (e.g., knowledge of B+ protocol, perceptions of care quality, care experiences at different clinics). The survey will be conducted in a private room and will take approximately 90 minutes.

Measured predictors will correspond to patient-level factors that reflect individual constructs, interpersonal relationships, and experiences with the health care facility (Figure 2) that may influence care engagement. These predictors were chosen based on meaningful influences that have been identified in prior research. The outcome of interest, postpartum HIV care engagement, will include receipt of ART (confirmed by clinical record review) and self-reported ART adherence with the ACTG adherence instrument,[47] using strategies to improve recall and validity.[48] We will implement mechanisms for retention (as Dr. Mmbaga has done for IMPAACT study). For women who are lost from the study, their care engagement data will be extracted from medical records.

At the 6-month postpartum visit, patient records will be reviewed to determine whether participants received viral load testing in the postpartum period as part of their standard of care. Women who have not received testing will be asked to provide a blood sample for viral load testing. The research nurse will perform the phlebotomy procedures. For HIV RNA, approximately 6 ml of whole blood will be collected in an EDTA tube. The collected samples will be stored at room temperature for not more than 4 hours and then transported to the KCRI biotechnology laboratory for analysis. HIV RNA samples will be analyzed in real time and results reported back to clinics. The samples of participants with observed viral loads greater than 1000 copies/ml will also be subject to resistance testing to assess the extent to which high viral loads are due to drug resistance.

Viral load and resistance test results will be shared with the patients in a timely manner. For participants who are still enrolled in HIV care in the study clinic, the results of their viral load and any resistance tests will be added to their medical record, to be discussed with the patient at their next clinical visit. For participants who are no longer in HIV care or who have transferred to another clinic, they will be called and informed that their viral load and any resistance test results are available and invited to come to the clinic to have them explained by the study nurse. For study purposes, the test results will be entered onto a clinical report form, marked only with the participant's study ID, and entered as part of the patient's study records. The results for the viral load and any resistance testing will be compared to self-reported adherence to inform analysis of viral suppression as a result of drug adherence versus drug resistance.

Eligibility: 200 female patients: Women who are ≥ 18 years of age, diagnosed with HIV, prescribed ART, and pregnant at the time of enrollment are eligible to enroll. Participants may either be newly initiating ART during pregnancy, or continuing ART due to an established HIV diagnosis. To ensure the safety of participants and integrity of the data, participants will be excluded if the attending physician determines that the patient has impaired mental status.

Recruitment: For female patients, the research nurses will work with a specific health care provider in the clinic to identify individuals who are eligible for the study. The heath care provider will approach the patient during a clinical appointment to see if she is interested in meeting with a research nurse to learn more about the study. If so, a research nurse will meet with the patient to explain the study and what participation involves, and to offer her the opportunity to participate if she chooses.

Compensation: At each survey, participants will receive 5,000 TSh (~3 USD) for participation.

Phase 3: Focus Group Discussions and In-Depth Interviews with Stakeholders

Procedure: We will conduct focus group discussions and in-depth interviews with the following populations: health care providers (IDIs/FGDs with 5 HIV care providers, PMTCT coordinators, and ANC nurses providing HIV testing); home-based HIV care workers (2 FGDs, 16 participants); HIV-infected pregnant and postpartum women (18 IDIs); and HIV-uninfected pregnant/postpartum women (12 IDIs). These discussions will identify opportunities to improve implementation of the national PMTCT policy to support continuous care engagement in the postpartum period and inform the content and protocol of the *Maisha* intervention. Semi-structured interview guides will be tailored to each group. Questions and probes related to intervention content (video and counseling) will focus on HIV stigma during two time points: presentation to ANC (e.g., HIV testing experience and current counseling, role of stigma upon HIV diagnosis, stigma for women with established diagnoses) and PMTCT initiation (e.g., content of PMTCT counseling, decision about care site, HIV disclosure). Questions and probes related to the study protocol will include: timing of recruitment, consent, and baseline; reactions to a video-based module; desired characteristics of intervention counselors; and strategies for retention. Interviews and FGDs will be audio-recorded with permission, and transcribed and translated into English. Intervention ideas will be further discussed and refined through a community stakeholder meeting.

Phase 4: Medical Record Review

A retrospective medical record review will include a review of the clinical records of all patients in antenatal care in the study clinics, who had deliveries in a two-year period, between Feb 1, 2014 (date of roll-out) and present. Data will be analyzed to first determine the proportion of pregnant women in ANC who had a documented HIV test result as part of ANC services, and of those, the number who were HIV infected (separately by new diagnoses and established diagnoses). For patients who are HIV-infected, a data extraction form will be used to merge information across the relevant clinical services (i.e., ANC, RCH, CTC). Linking patients across the three registries will be possible by linking the unique Tanzanian CTC identification number that is given to all patients upon initiation of ART. The data extracted from each setting are described in Table 2.

Table 2: Data extracted from the clinical records of HIV-infected pregnant patients

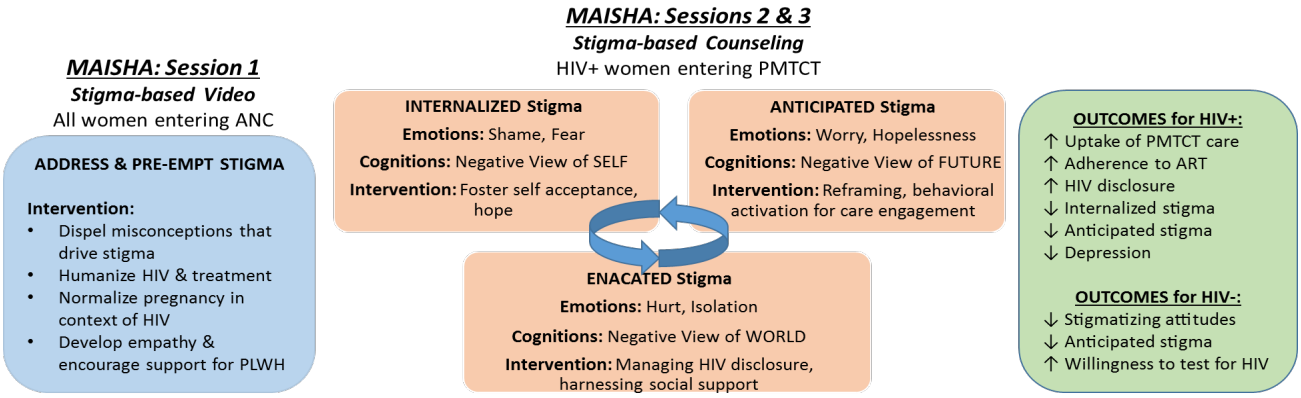
ANC	Socio-demographics HIV testing history Counseling exposure ART initiation Engagement in care
RCH	Delivery data Counseling exposure Engagement in care Referral to CTC
CTC	Linkage to CTC (ever, date, location) Counseling exposure Engagement in care Viral load

Phase 5: Development of the *Maisha* Intervention

Procedure: Intervention development will begin during the qualitative procedures described in Phase 3, which will allow for an iterative process where new data collection builds upon what has

been learned, continually making progress to finalize intervention and protocol content. We will also conduct ~40 observation hours in each of the two clinic sites selected for the pilot trial and record detailed notes on clinic flow and opportunities to integrate study activities into routine care. During this phase, we will also use various methods to confirm and refine our measurements of HIV stigma. Cognitive interviews[49] will assess whether our stigma measures capture the constructs of stigmatizing attitudes, internalized stigma, and anticipated stigma in this population, and whether items are appropriate, comprehensible given literacy levels, culturally salient, and translated to reflect the desired constructs. Per typical measure development procedures,[50] we will conduct cognitive interviews with 10 HIV-infected pregnant or recently postpartum women identified during Phase 3 IDIs. Detailed notes will be taken during the cognitive interviews and discussed as a team in order to finalize the measures and their translations.

Figure 3. Intervention Theoretical Framework



The Phase 3 qualitative data and the theoretical framework (Figure 3) will be used to create intervention content for three counseling sessions. For session 1, we will write a script with accompanying visuals that will then be adapted to a video format. The video will be recorded in Tanzania, with support from a video consultant in Moshi, who will oversee the recording and final editing of the video. Depending on the qualitative input, video content may include actual people living with HIV, health care providers, and general community members – all with the goal of normalizing HIV and creating an environment of support and empathy for PLWH. For sessions 2 and 3, we will develop a semi-structured curriculum that includes session descriptions, activities, and psychoeducation, and links back to the video content. We will get feedback on the draft intervention via a half-day study advisory board meeting and a trial run with 6 participants. The intervention facilitators will be trained and will conduct the trial run. Debriefing interviews with intervention counselors and trial run participants will elicit areas for modification and counselor training. The feedback will inform final modifications to the intervention content, and the final video will be revised as needed.

Phase 6: Pilot RCT of the *Maisha* Intervention

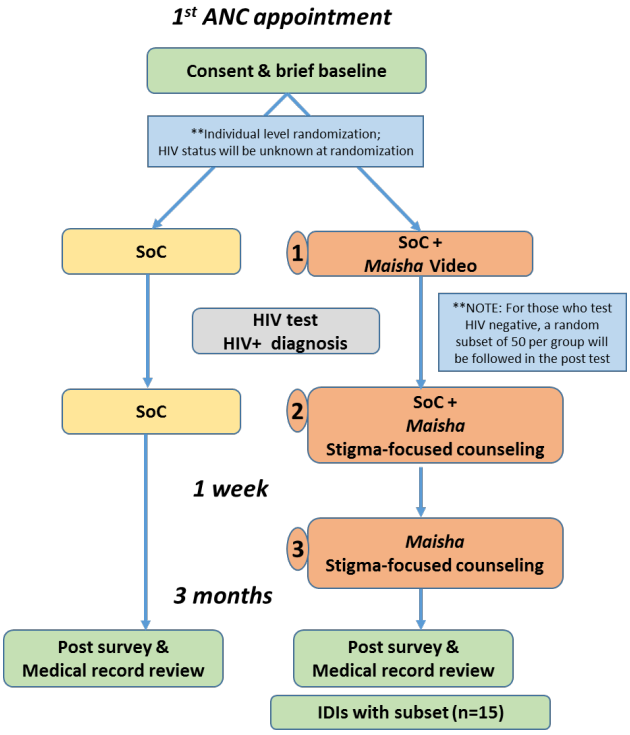
Procedure:
For the full pilot test of *Maisha,* female ANC patients who are interested in enrolling in the study will be orally administered the informed consent by the study researcher. Participants will then complete an interviewer-administered, structured baseline survey. The survey will include questions about demographics, social support, attitudes toward HIV and people living with HIV, HIV testing history, and mental health. Following the baseline survey, participants will be randomized to receive either the control condition (standard of care) or the intervention condition (standard of care + *Maisha)* (Figure 4).

Participants assigned to the control condition will receive the standard of care at the clinic, which includes all standard procedures related to HIV counseling.

Participants assigned to the intervention condition will receive the *Maisha* Session 1 counseling intervention (video, followed by a brief counseling session) immediately following the baseline survey, in the same private meeting space. They will then return to the waiting area to await the standard of care for the first ANC visit (which includes HIV testing). At this time, the study researcher will inform the clinic nurse that the participant is a part of the intervention condition.

Upon completion of the standard of care HIV counseling and testing, participants who are HIV-positive will be escorted by clinic nurses back to the study researcher's office to immediately complete the *Maisha* Session 2 counseling session. At the conclusion of this session, the participant will be invited and encouraged to attend a Session 3 individual counseling session at the same location 1 week later.

Figure 4. Pilot test design



3 months after baseline, all HIV-positive participants (expected n=50) and a sub-set of 100 HIV-negative participants will complete a follow-up survey. The survey will explore key constructs reflecting health outcomes (HIV care engagement, adherence to ART, mental health), stigma outcomes (internalized, anticipated, and enacted stigma), and secondary outcomes (social support, partner support, intimate partner violence). This survey will be conducted in a private room and will take approximately 60 minutes.

Immediately after the 3-month survey, a subset of 15 HIV-positive intervention participants (5 established diagnoses, 10 new diagnoses) will be invited to participate in a qualitative in-depth interview (IDI) to explore their reactions to the intervention with greater nuance. Interviews will be conducted immediately after the survey and will take an additional 60 minutes. The IDI will be conducted in Kiswahili, using a semi-structured guide. Interviews will be audio recorded with participants' permission.

At the conclusion of pilot trial participation, the research nurse will review the medical records of the 150 pilot trial participants who are selected to receive follow-up as part of the study. A structured data extraction form will be used to record key data on HIV care engagement.

2. Subject Selection

Below are the eligibility and recruitment procedures that the KCMC team will use for inclusion of participants by study phase.

Phase 1: Key Informant Interviews with Health Care Providers

Eligibility: 30 health care providers: Individuals who are employed at one of the three study clinics and are involved in the care of HIV-infected women who are pregnant or postpartum. These individuals may include nurses, counselors, physicians, data capturers, and managers.

Recruitment: For health care providers, the KCMC PI (Dr. Mmbaga), the Duke graduate student and KCMC research nurses will conduct a brief presentation at each of the study clinics. The research nurse and the Duke graduate student will then approach providers individually to invite them to participate in a key informant interview.

Phase 2: Surveys and In-depth Interviews with female patients

Eligibility: 200 female patients: Women who are ≥ 18 years of age, diagnosed with HIV, prescribed ART, and pregnant at the time of enrollment are eligible to enroll. Participants may either be newly initiating ART during pregnancy, or continuing ART due to an established HIV diagnosis. To ensure the safety of participants and integrity of the data, participants will be excluded if the attending physician determines that the patient has impaired mental status.

Recruitment: For female patients, the KCMC research nurses will work with a specific health care provider in the clinic to identify individuals who are eligible for the study. The health care provider will approach the patient during a clinical appointment to see if she is interested in meeting with a KCMC research nurse to learn more about the study. If so, a research nurse will meet with the patient to explain the study and what participation involves, and to offer her the opportunity to participate if she chooses.

Phase 3: Focus Group Discussions with Stakeholders

Eligibility:

- Health care providers, 3 FGDs or IDIs with 5 participants: Individuals who are employed at the study clinics and are involved in the care of HIV-infected women or women testing for HIV who are pregnant or postpartum. These individuals may include nurses, counselors, physicians, social workers, nursing assistants, data capturers, and managers.
- Community health workers (CHWs), 2 FGD, 16 participants: CHWs are based in the study clinics to provide community-based care and support for people living with HIV (PLWH), and to encourage and coordinate HIV care engagement.
- HIV-infected pregnant/postpartum women, 18 IDIs: Women who are ≥ 18 years of age, diagnosed with HIV, prescribed ART, and pregnant or within 6 months postpartum at the time of enrollment. Participants may either be newly initiating ART during pregnancy, or continuing ART due to an established HIV diagnosis. To ensure the safety of participants and integrity of the data, participants will be excluded if an attending clinician determines that the patient has impaired mental status.
- HIV-uninfected pregnant and postpartum women, 12 IDIs: Women who are > 18 years of age, pregnant or within 6 months postpartum, and received a negative HIV test result during pregnancy.

Recruitment: For health care providers, the KCMC PI (Dr. Mmbaga), the Duke graduate student and KCMC research nurses will conduct a brief presentation at each of the study clinics. The research nurse will then approach providers individually to invite them to participate in a key informant interview. For female patients, the Duke graduate student and KCMC research nurses will work with a specific health care provider in each clinic to identify individuals who are eligible for the study. The heath care provider will approach the patient during a clinical appointment to see if she is interested in meeting with a research nurse to learn more about the study. If so, a research nurse will meet with the patient to explain the study and what participation involves, and to offer her the opportunity to participate if she chooses.

Compensation: Patients will receive 5,000 TSh (~3 USD) for participation, and providers will receive an equivalently valued gift for participation.

Phase 5: Development of the *Maisha* Intervention

Eligibility: HIV-infected pregnant/postpartum women: Women who are > 18 years of age, diagnosed with HIV, prescribed ART, and pregnant or within 6 months postpartum at the time of enrollment.

Participants completing cognitive interviews may be the same as those completing IDIs in Phase 3. 6 additional women will be enrolled for a trial run of the *Maisha* intervention.

Recruitment: The research nurses will work with a specific health care provider in the clinic to identify individuals who are eligible for the study. The heath care provider will approach the patient during a clinical appointment to see if she is interested in meeting with a research nurse to learn more about the study. If so, a research nurse will meet with the patient to explain the study and what participation involves, and to offer her the opportunity to participate if she chooses.

Compensation: Trial run participants will receive 10,000 TSh (~6 USD) per visit for participation. Cognitive interview participants will receive 5,000 TSh (~3 USD) for their participation.

Phase 6: Pilot RCT of the *Maisha* Intervention

Eligibility: 1000 female patients: Women who are > 18 years of age, pregnant, and attending their first ANC appointments for the current pregnancy at one of the two pilot test study sites are eligible to enroll. To ensure the safety of participants and integrity of the data, participants will be excluded if the attending physician determines that the patient has impaired mental status.

Recruitment: Research staff will work with clinic staff, including the receptionist at the Reproductive & Child Health (RCH) clinic and the ANC clinic nurse-in-charge, to identify women who are eligible for the study. When a woman arrives for her ANC appointment, she is routinely asked whether this is her first clinic appointment for the current pregnancy. For all women who answer “yes” to this question, the intake nurse will inform her that there is a research study taking place and inquire whether she would like to speak to the study researcher. Those who agree will meet with the study researcher, who will explain the study, review eligibility criteria, and offer her the opportunity to participate if she chooses, following the informed consent procedures. Clinic staff will be given a small monthly stipend to compensate for the added work of identifying and referring interested clients to the study staff; they will *not* be reimbursed based on whether or not the referral is successful, so that compensation does not create undue influence on a patient’s participation in the study. Enrollment will stop when we have enrolled 50 women who are HIV infected, which we estimate will require consenting and baselining approximately 1000 women over a six month period.

Compensation: No compensation will be offered at baseline, but nutritious snacks will be given to all women taking part. Women who attend a follow-up counseling session will receive 5000 TSh (~3 USD) to cover their transportation. Women who complete a 3-month survey will receive 5000 TSh for their participation, and snacks will be offered during the assessment. Women who complete an in-depth interview will receive an additional 5000 TSh.

3. Risks and Benefits

The risk/benefit ratio for this study is relatively low, primarily because all of the data collection procedures are minimally invasive. All procedures will be performed by trained research staff at KCMC and the Duke graduate student, who will follow protocols to minimize risks, discomfort, and adverse events. As an implementation science study, we expect that the results of this study will inform the delivery of HIV care services for women in this setting. Women who receive the counseling intervention as part of the trial run or pilot test may also receive benefits associated with the counseling. At Duke, the primary risks will be confidentiality of the data we receive. The procedures to protect confidentiality of the data are described below.

We believe that the potential risks of this study are reasonable given the potential benefits to inform future service implementation. The study team at KCMC has significant experience working with this population, and we are confident in their assessment of potential risks and their ability to

handle such risks. They are also well-equipped to supervise the Duke graduate student in her role with the support of the Duke co-PI. As such, we believe that the potential benefits outweigh the risks posed to human subjects. This research is expected to yield important new information on the implementation of Option B+ in Tanzania, which can inform the delivery of services in Tanzania and similar settings.

4. Confidentiality

Confidentiality is of critical importance, and we will take many precautions to protect against the possibility of a breach of confidentiality at Duke. Our research team is very aware of the importance of maintaining strict confidentiality and has extensive experience dealing with sensitive information. At KCMC, the team has developed a study protocol to protect the confidential information collected from human subjects; this ethics protocol has been approved by KCMC and NIMR.

Transfer of Digital Data from KCMC to Duke University
The KCMC study team will collect the assessment data via paper and pencil and will enter the data into a RedCap software program that is programed at Duke. Duke will access the data by logging in to the secure RedCap server. If other data or study related information that has sensitive health information is shared with Duke, it will be transferred via a "sensitive data" project folder that will be established for this project on box.duke.edu (PROJECT_DGHI_PMTCT). Limited members of the study team at Duke will have access to the Duke Box folder. Within one week of data upload, authorized team members at Duke will move the data from the shared box.com folder to a folder on the protected server that will be established for the project (\\secure-nas-fe01.oit.duke.edu\chpir\projects\PMTCT-watt). The data will be stored on Box, and relevant Duke study staff on the IRB protocol will access the drive through a VPN connection. De-identified data will remain on Duke Box when required for cross-site collaborations (e.g., data analysis). Otherwise, the data will be deleted on Duke Box.

The study team will also host a Dropbox folder and use email to share materials that are essential to the study progress, but that do not contain participant data. Such materials may include study protocols, data collection instruments, and participant tracking logs that include participant ID and survey assessment dates. Materials shared through these means will not include names, contact information, clinic visit dates, or any participant-level data.

Storage of Digital Data at Duke University
All data kept at Duke University will be stored electronically, either on Duke Box or on the secure, password protected server folder that will be established for this study (\\secure-nas-fe01.oit.duke.edu\chpir\projects\PMTCT-watt). Quantitative data will be stored as SPSS files and we will use SPSS to analyze the data. Qualitative data will be stored as Microsoft Word documents and NVivo project files, and we will use NVivo to analyze the data. The server where the data is stored meets all requirements for handling sensitive health data, as outlined in the Duke ITSO server standard security document. Only research staff who have completed IRB training and are directly involved in this project will have access to the data. The IT person responsible for managing the Duke team's access to the server is Patrick Daniels, IT Manager – West Campus/Trent Support, (919) 660-2401.

All study data will be kept identified by a study ID number. The file linking the participant ID number and identifying information of the individual (name, contact information) will be stored in a locked cabinet in Moshi, Tanzania. The Duke study team will not have access to that file.

5. Trainee Supervision

The research team at KCMC, led by the Co-PI, Dr. Blandina, will be involved with orientation, training and supervision of students and trainees involved in the study. This will be done with the support of the study team at Duke University. The KCMC team will also provide the trainees with resources needed to facilitate their involvement in the project(s) (e.g., workspace, equipment, access to data, etc.), meet regularly with them to provide support, guidance, and feedback and communicate with the Duke team to provide feedback on their progress.

6. Compensation

Below we describe the compensation procedures that KCMC will use for participants by study phase. Under all circumstances, participants who begin a procedure will receive compensation, even if they voluntarily choose not to complete the procedure.

Phase 1: Key Informant Interviews with Health Care Providers

Compensation: Participants will receive a small gift valued at 5,000 TSh (~3 USD) for participation. With the guidance of the Ministry of Health, it was determined that compensation in the form of a gift would be more appropriate than cash.

Phase 2: Surveys and In-depth Interviews with female patients

Compensation: Participants will receive 5,000 TSh (~3 USD) for participation in each survey assessment and in-depth interview.

Phase 3: Focus Group Discussions and In-Depth Interviews with Stakeholders

Compensation: Patients will receive 5,000 TSh (~3 USD) for participation, and providers will receive an equivalently valued gift for participation.

Phase 4: Medical Record Review
No human subjects to compensate.

Phase 5: Development of the *Maisha* Intervention
Compensation: Trial run participants will receive 10,000 TSh (~6 USD) per visit for participation. Cognitive interview participants will receive 5,000 TSh (~3 USD) for their participation.

Phase 6: Pilot RCT of the *Maisha* Intervention
Compensation: No compensation will be offered at baseline, but nutritious snacks will be given to all women taking part. Women who attend a follow-up counseling session will receive 5,000 TSh (~3 USD) to cover their transportation. Women who complete a 3-month survey will receive 5,000 TSh for their participation, and snacks will be offered during the assessment. Women who complete an in-depth interview will receive an additional 5,000 TSh.

7. Informed Consent

Prior to participating in the study, KCMC staff and the Duke graduate student will obtain informed consent from participants. A KCMC research assistant and the Duke graduate student will describe the study in detail to the participant, allow him/her ample time to read the consent form thoroughly (or have it read to them) and ask questions, and ensure that he/she understands the purpose of the study, study procedures involved, and potential risks. Verification of comprehension of informed consent will be accomplished by asking participants to recall central points in the consent process. This procedure will also provide an opportunity to clarify any points of confusion. Participants will complete a separate informed consent for observations of their medical care at the clinic. Participants will sign one copy of the informed consent form and will be given a copy for their

personal records. If the participant is not able to write his/her name, a thumb print can be used in lieu of a signature. Participants will be told at enrollment that their decision to participate or not will in no way affect their current or future employment or health care at the facility.

8. Deception

N/A. This study does not involve deception.

9. Debriefing

N/A. Because this study does not include deception, it is not necessary to conduct debriefing (defined by the IRB as telling the subjects about the deception).

10. Statistical analysis

Data analysis for Aim 3 (pilot trial) will follow guidelines of the CONSORT 2010 statement, as extended to pilot feasibility trials.

Feasibility and acceptability of the intervention and the associated trial will be described by: recruitment and retention patterns, participant satisfaction, fidelity, and implementation cost. Retention will be monitored to calculate the percentage of participants who attend the 1-week *Maisha* session (in intervention) and the 3-month assessment, to document barriers to attendance for participants, and to examine differences between those who attend and those who do not. Participant satisfaction data at the 3-month follow-up will be described, with >80% satisfaction used as a metric of acceptability. Qualitative data will be thematically coded for focus on participants' perceptions of the intervention, suggestions for changes, and feasibility moving forward. The fidelity to the intervention will be assessed by examining the percentage of components from the manualized content that are covered in each session. To estimate the cost of the intervention, we will track the time for training and delivery, as well as actual costs incurred. Qualitative feedback and QA data will be used to revise and improve the curriculum for the future.

Potential efficacy will be examined by analyzing separate outcomes for HIV-infected and HIV-uninfected women. For HIV-infected women, we are interested in differences between conditions in health outcomes (retention in PMTCT, medication adherence, depression) and stigma (anticipated stigma, internalized stigma and HIV disclosure). For HIV-uninfected women, we are interested in differences between conditions in stigma (attitudes to PLWH and anticipated stigma), as well as willingness to test for HIV in the future. For outcomes where there is a baseline measure, mixed-effects regressions will be used to model pre-post differences within and between arms, using a time by condition model specification (time, condition, and time*condition). Individual-level random intercepts will be used to account for correlation due to repeated measurement. Using a mixed-effects regression approach leaves flexibility to control for baseline outcome values that may not be balanced between groups due to small sample size, and may improve precision of treatment effect estimation. For outcomes where there is no baseline measure, we will examine differences in means or proportions with 95% confidence intervals. If we suspect, a priori, that baseline imbalance in prognostic covariates may be an issue, we will move into a regression framework. Results across outcomes will generate parameter estimates and potential ranges of values to estimate power for a future R01. This analytic approach is consistent with best practices for analysis of pilot feasibility trials. Data analysis will be led by the KCRI statistician and DGHI postdoc. To reduce bias and ensure reproducibility of results, we will discuss analytic approaches and review syntax as a team. All outcome analysis will be reviewed by an external statistician with study condition blinded (see letter from DGHI Research Design Core).

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