Study Protocol

Official study title: Understanding the Role of Food Insecurity and Depression in Non-adherence to Option B+ Among Perinatal Kenyan Women Living With HIV: A Syndemics Approach

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Note: This study protocol describes 2 phases of the study. The Intervention Pilot registered with ClinicTrials.gov, with the brief title "Healthy Mothers: an Intervention to Support Perinatal Women Living With HIV in Kenya", is part of Phase 2—described beginning on line 327.

1. Title: Understanding the role of food insecurity and depression in non-adherence to Option B+ among perinatal Kenyan women living with HIV: a Syndemics approach.

2. Investigators and Institutional Affiliations

Name	Organization	Role on Project
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Collaborating institutions moved as appendix

List of Abbreviations
ART: Antiretroviral Therapy
HIV: Human Immunosuppression Virus
FI: Food Insecurity
PMTCT: prevention of mother to child transmission of HIV
EBF: exclusive breastfeeding

3. ABSTRACT

Strategies to prevent mother-to-child transmission (PMTCT) of HIV can reduce the risk of vertical transmission to less than 2%, but difficulties in adhering to the three pillars of PMTCT (maternal ART; exclusive breastfeeding; provision of ART prophylaxis to infant) has led to high rates of MTCT in sub-Saharan Africa and suboptimal maternal and infant health. The goals of the proposed research are to: 1) gain an understanding of the influences and mechanisms by which food insecurity (FI) and perinatal depression- two modifiable determinants of non-adherence to HIV treatment and exclusive breastfeeding- interact to impact adherence through a qualitative approach, and 2) Develop and pilot test a theory-based intervention that bolsters adherence to the PMTCT guidelines.

Methods: To better understand the relationship of food insecurity and depression among pregnant and postpartum women living with HIV we will use a longitudinal qualitative design. Thirty pregnant women will be recruited in their third trimester to participate in an in-depth interview. Each participant will be followed up to 12 months postpartum and asked to participate in three additional interviews in order to understand how depression changes over time (each participant will participate in a total of 4 interviews over this timeframe). Drawing upon findings from the in-depth interviews, in conjunction with key informant interviews (n= 5-up to 12) and focus group discussions with our target population (1-2 discussions with n=8-12 participants), we will apply the theoretical model of transitions theory to develop a multi-level intervention that improves adherence to PMTCT guidelines. We will test intervention acceptability and feasibility among 40 pregnant women (20 intervention and 20 current standard of care) and conduct follow-up to evaluate results at 6-months postpartum. **Candidate and Mentoring:** This project is being supported by an NIH K23 Career Development Award. I am a nurse-scientist with a background in health behavior change theory and infant feeding in the context of HIV. My mentor team is composed of exceptional research scientists from multiple disciplines with extensive experience in HIV treatment and prevention research in Kenya.

4. INTRODUCTION/BACKGROUND

In 2016, 160,000 children acquired HIV from mother to child transmission of HIV; 90% of these occurred in sub-Saharan Africa (SSA), including Kenya [1]. PMTCT is now entirely possible through the efficacious strategies in Option B+ which include: [2-6] 1) women with HIV be placed on lifelong antiretroviral therapy (ART), 2) women are advised to exclusively breastfeed (EBF) their infant for the first 6 months of life, and 3) provision of prophylactic HIV treatment to the HIV-exposed infant throughout the breastfeeding period. However, suboptimal engagement in care and inadequate ART adherence during pregnancy and, especially postpartum remain major concerns and compromise the ability for women to remain adherent to lifelong ART[5,7-9]. On average, 50%, with some studies finding as high as 81% of HIV+ mothers [10,11] are disengaged in care by 6 months postpartum, suggesting non-adherence to Option B+[12,13]. As such, although adhering to PMTCT Option B+ reduces the risk of MTCT of HIV from 45% to less than 2%[14], HIV incidence among children born to mothers living with HIV remains unacceptably high[11]. For instance, in Kenya, MTCT rates are approximately 14%[15]. Furthermore, non-adherence to Option B+ increases morbidity and mortality for mothers[16] and their infants[17] and prevents both mothers and infants from the health and nutritional benefits of EBF[18-20]. **In effect, we have solved PMTCT efficacy. We have not solved Option B+ implementation effectiveness** and furthering maternal and child health for HIV+ mothers. In order to fully realize the benefits of Option B+ and fill a crucial knowledge gap, it is necessary to identify and address drivers of Option B+ non-adherence[21].

Two potential drivers of non-adherence to Option B+, that are also substantial health issues in SSA, including in Kenya, are food insecurity (FI) and perinatal (pregnancy and postpartum) depression. In SSA, over half of people living with HIV are moderately or severely food insecure [22]and rates of depression among all pregnant and postpartum women range from 10-47% [23]. FI is inextricably linked with poor health outcomes among people living with HIV, including increased disease progression, lower ART adherence [24,25], and higher mortality [26]. Perinatal women are uniquely vulnerable to FI due to nutrient demands being higher, the effort required to prepare food, and financial constraints related to being obliged to leave the workforce[27]. FI during pregnancy is associated with poor pregnancy outcomes, including low birth weight and gestational diabetes [28,29], and increased risk of MTCT[25]. Postpartum FI can impact breastfeeding outcomes[30], child cognitive development [31] and increase the risk of MTCT of HIV [32].

In separate studies among women living with HIV, depression has been associated with poor adherence to ART [17,33-37] and EBF practice [38-40], as well as the risk of MTCT of HIV[41,42]. FI is an important driver of depression[27,43]. A cross-sectional study found that FI was associated with maternal depression among all women across four ethnic groups in Tanzania [44]. The authors proposed several explanations; FI can lead to poor diet exacerbating anxiety and depression; FI can lead to feelings of disempowerment increasing depression; and both FI and depression share roots in larger inequalities preventing women from economic opportunities [44].These data show FI and depression are interrelated and burden perinatal women[45].

Interventions to improve Option B+ adherence by targeting FI and perinatal depression simultaneously have the potential for greater success, but are lacking[4,13,46-49]. Existing interventions to improve PMTCT have focused almost exclusively on supporting adherence to one of the three pillars. In Kenya, Drake et al., applied a novel mHealth strategy to improve postpartum adherence to ART[46]. Fayorsey et al., utilized a combination of support strategies including, phone and messaging, counseling and follow up support in the case of missed-appointments [50] to increase retention in care and adherence. Other interventions have focused on the EBF pillar of the PMTCT cascade [51,52] through peer counselors [53] or clinic-based counseling sessions [54]. Interventions to improve PMTCT must account for the multiple levels of influence that facilitate or inhibit HIV treatment and EBF success throughout pregnancy and postpartum, yet few do.

5. JUSTIFICATION FOR THE STUDY

Current Research Gaps: Although existing literature provides evidence linking FI and perinatal depression among HIV+ women, there is a crucial gap in understanding the detrimental synergy in the interplay between these two factors and their combined impact on Option B+ adherence[27,55,61,62]. In addition, understanding maternal retention to Option B+ adherence beyond 6-weeks postpartum is extremely limited[49]. A sharp drop-off in engagement of mothers and their infants occurs after 6 weeks, yet the reasons for this are unclear. This compromises Option B+ adherence and long-term health as women fail to return for ART refills, infant HIV testing, or infant feeding follow-up. Longitudinal data are needed to help understand this trend. Moreover, theory-based approaches to mitigate non-adherence among postpartum HIV+ women are lacking[66] and none have focused on addressing FI and depression together.

Findings from phase one of our study demonstrated that financial insecurity during the perinatal period was detrimental to the mental health and food security of mothers living with HIV,[82] and cash transfers have been shown to improve outcomes for low-income families in Kenya.[83,84] Yet, little is known about the specific benefits of cash transfers to perinatal women living with HIV (WLWH) and their infants in this setting. In addition, participants from phase one also reported challenges, including significant stress, related to safe infant feeding, a key component of the prevention of mother to child transmission strategy. Barriers to current infant feeding guidelines (specifically EBF for the first 6-months postpartum) are now well documented,[85-90] however, more research is needed to develop and test interventions that support women to overcome these barriers.

6. HYPOTHESIS

Hypothesis 1: We hypothesize that higher levels of food insecurity and depression lead to lower adherence to prevention of mother to child transmission of HIV strategies. These strategies include HIV treatment for the mother, treatment for her infant and to exclusively breastfeed for 6 months.

Hypothesis 2: We hypothesize that targeted support provided to women living with HIV during the transition period from pregnancy to postpartum can improved adherence to the prevention of mother to child transmission of HIV guidelines.

6b. Theoretical framework Under the mentorship of Dr. Weiser, we developed a conceptual framework to serve as a basis for the research proposed here. This framework draws from Weiser et al.'s framework illustrating the relationship between FI and HIV/AIDS outcomes. The original framework posits that FI and HIV/AIDS are linked in a harmful cycle through nutritional, mental health and behavioral pathways among people living with HIV[63]. In this proposal, we apply these underpinnings to the complex relationship between FI and depression during the perinatal period and its impact on both PMTCT outcomes and maternal and infant health (Figure 1). Our framework draws on Syndemic Theory[64], the co-occurring conditions of poverty, depression and HIV resulting in a synergistic response worsening the effects of each state. As can be seen in Figure 1, I hypothesize that FI operates at the household level to impact perinatal depression. In turn, perinatal depression acts through several mechanisms, including perinatal stress, lack of self-efficacy and lack of social support to influence adherence to PMTCT strategies and maternal and infant health. Moreover, our model stresses that both FI and perinatal depression operate independently and jointly to impact maternal health. Previous work has demonstrated the link between stress, self-efficacy and social support and poor maternal outcomes postpartum[65-67], however the role and the interplay of FI and perinatal depression among HIV+ women over time remains a knowledge gap we hope this proposal will start to fill.

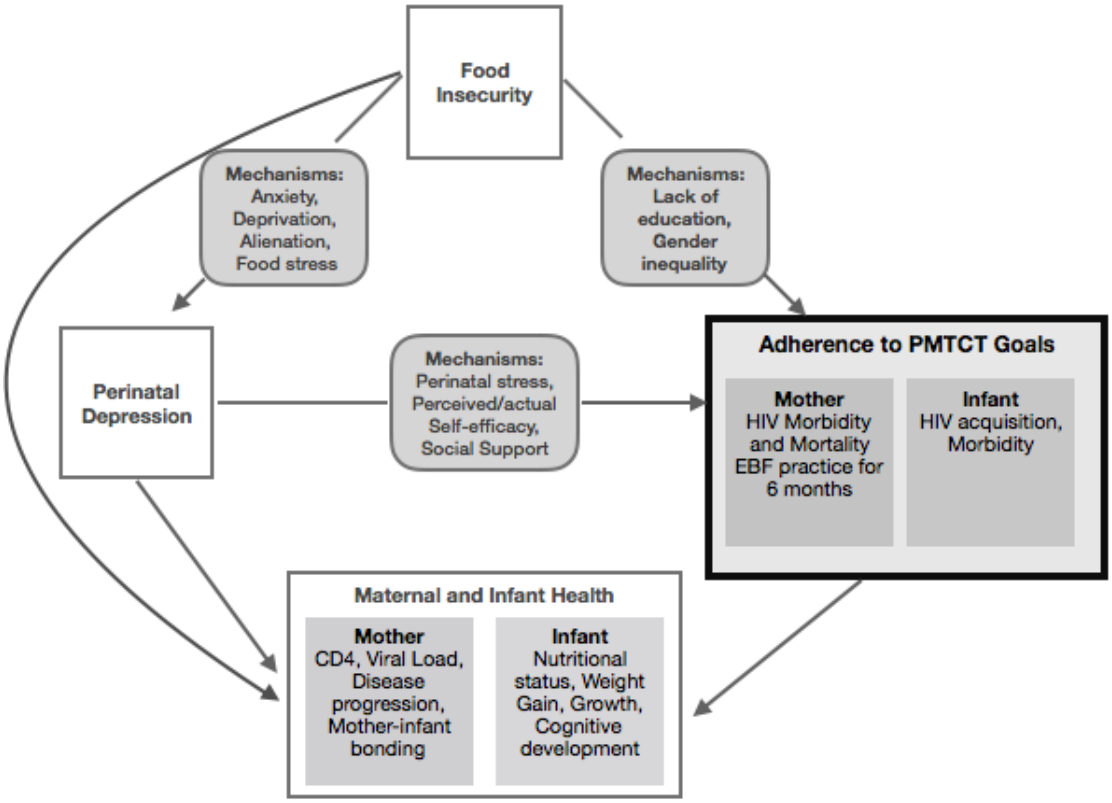

Figure 1: Conceptual framework for food insecurity, depression and PMTCT linkages

In addition to the conceptual framework we have developed, Transitions Theory provides an innovative framework to explore HIV treatment adherence among pregnant and postpartum women.[75] The theory was developed by Dr. Afaf Meleis who recognized healthy and unhealthy patterns in the way people experience and respond to different life transitions.[76] According to the theory, transitions occur over a period of time, they are characterized by change and adaptation and, once complete, result in a state of greater stability relative to the period of transition during which established support systems and resources may have been disrupted.[77] We will apply transitions theory[35] (making this the first study to apply a targeted theory to understand the experiences of postpartum women living with HIV) with the aim of improving PMTCT adherence. Our intervention development will adapt the Transition's Theory framework to target the specific personal, community, and societal issues identified by participants in the in-depth interviews.

7a. GENERAL OBJECTIVES

The proposed study will investigate the role of food insecurity and depression among women living with HIV and its impact on adherence to HIV treatment and prevention strategies as well as develop and test the acceptability and feasibility of a multi-level FI and depression intervention for perinatal HIV+ women in Kenya.

7b. SPECIFIC OBJECTIVES

1. **Phase One: Identify factors that increase risk for or protect against FI and perinatal depression among HIV+ women in the Nyanza Region of Kenya** We will use qualitative techniques to clarify the protective factors, perceived causes, cultural understandings and individual perspectives of FI and perinatal depression by conducting a longitudinal design with in-depth interviews at 4 consequential time-points (i.e., prenatal, 1, 4 and after 6-months postpartum) with 30 HIV+ women who screen positive for depressive symptoms during routine care visits in Kisumu, Kenya. Our sample size is based on previous qualitative work where data saturation was reached with less than 30 participants. Applying grounded theory analysis techniques, I will describe how the above factors and perspectives of FI and depression are manifested in the perinatal period.

2. **Phase Two: Apply findings from Phase One, using the theoretical framework of Transitions Theory to develop and test the acceptability and feasibility of a multi-level intervention to promote adherence to PMTCT strategies for perinatal HIV+ women in Kenya.** Drawing upon findings from Phase One of our study, in conjunction with consultation with key informant interviews with FACES clinic staff (n=5-12) and focus group discussions with our target population (1-2 discussion with n=8-12 participants per group), we will apply the theoretical model of transitions theory to develop a multi-level intervention that improves adherence to PMTCT guidelines. The intervention will be tested among 40 pregnant women (20 intervention and 20 current standard of care) and follow-up to evaluate results will occur at 6-months postpartum. The intervention will likely include individual mental health and nutrition counseling, and food support with or without some livelihood training.

   In Phase One of our study, we identified perceived or actual milk insufficiency, as primary barrier to exclusive breastfeeding not addressed through the current education and support being provided at the clinic. Furthermore, we identified financial insecurity as a deeply-rooted threat to the health and well-being of perinatal WLWH and their infants across time. Based on our findings from our longitudinal qualitative study, our key informant interviews, focus groups with our target population and a review of the literature, we developed an intervention which we will pilot test to determine the potential impact of providing individualized support from a local lactation specialist along with monthly unconditional cash transfers (UCTs) to WLWH from 20-35 weeks pregnancy to 6-months postpartum.
   The pilot test will be carried out among 40 pregnant women divided into 2 groups (n=20 intervention group, n=20 control group). The intervention group will receive personalized lactation support and monthly UCTs from approximately 30 weeks pregnancy to approximately 6-months postpartum. Personalized lactation support will be provided by a local, experienced lactation consultant. Her support will be aimed at providing person centered care to assess for and address barriers to optimal, safe infant feeding with a focus on exclusive breastfeeding for the first 6-months postpartum. The cash transfer will be 10,000 Kenyan shillings per month. This amount is slightly less than the median amount women in our preliminary study reported needing to meet their basic needs (13,500KES) and is in line with other cash transfers completed in the area.[83] It is equivalent to approximately 3.33USD per day, or about 40% more than the World Bank's most recent poverty line estimated of 1.90 USD per person per day. This amount is lower than the estimated median

monthly income for those informally employed in sectors such as retail trade or food service in Kenya (estimated at 15,000 and 30,000KES monthly in rural and urban areas respectively).[91] We expect this amount will allow women to meet many of their household's basic needs during late pregnancy and throughout the period of EBF when women are largely unable to maintain gainful employment.

The control group will receive the current standard care.

We will recruit women during their 20th-35th week of pregnancy and follow them until 6-months postpartum. We will collect survey and clinical data at baseline (20-35 weeks pregnancy, 2-weeks, 4-weeks, 6-weeks, 3-months and 6-months). We will conduct qualitative interviews at the end of the intervention period with all 20 participants in the intervention group to evaluate the acceptability of the pilot intervention as well as to better understand how UCTs were used and the perceived impact on financial security, food security, mental health, relationships with primary partners and the ability to adhere to PMTCT strategies.

8. DESIGN AND METHODOLOGY

Phase One (In-depth Interviews):

(a) Study site (geographical): The proposed study will be conducted in Kisumu county in the former Nyanza Region in western Kenya.

Table 1: Characteristics of study population	
	Aim 1: Longitudinal Interview
Sample Size	N= 30 women to complete 4 interviews each (Number of interviews=120)
Age	18+
Inclusion Criteria	32-38 weeks pregnant at enrollment Depressive Symptoms: two-thirds of the sample- Screen positive for depressive symptoms on PHQ-9 scale and one-third who screen negative for depressive symptoms HIV positive Currently prescribed ART
Exclusion Criteria	High-risk pregnancy for reasons other than HIV status (e.g., pregnancy complications, preeclampia, gestational diabetes, preterm labor) Self-reported participation in another ART adherence-related study Unable to understand consent process Planning on relocating out of Nyanza province over the next 12 months

(b) Study populations: Pregnant and postpartum women over 18 years of age.

(i)Inclusion criteria: 1) 32-38 weeks pregnant at enrollment, 2) Depressive Symptoms: two-thirds of the sample- Screen positive for depressive symptoms on PHQ-9 scale and one-third who screen negative for depressive symptoms, 3) HIV positive and 4) Currently prescribed ART.

(ii)Exclusion criteria: 1) High-risk pregnancy for reasons other than HIV status (e.g., pregnancy complications, preeclampia, gestational diabetes, preterm labor), 2) Self-reported participation in another ART adherence-related study, 3) Unable to understand consent process, and 4) Planning on relocating out of Nyanza province over the next 12 months.

(c) Sampling

(i) Sample size determination: For Qualitative Interviews (Aim 1), we will recruit a sample of N=30 HIV positive pregnant women to complete four in-depth interviews over the course of approximately one year. We anticipate this sample size will reach saturation, which will be assessed on an on-going basis based on previous qualitative work. The sample size has been increased from the original protocol to account for attrition which may occur during the time between follow up interviews such that we can ensure saturation is reached despite some anticipated loss to follow up. We will recruit through designated FACES clinics in-person with a FACES staff member positioned in the clinic waiting room. Interested women will be assessed for eligibility using a brief screening assessment administered by a female study staff member.

(ii) Sampling procedures: See above

(d) Procedures

(i) Description of the type of data to be collected and collection procedures: We will enroll 30 HIV+ pregnant women recruited from FACES to complete 120 in-depth interviews (4 per participant). We anticipate this sample size

will reach saturation, which will be assessed on an on-going basis. Each interview will last 1-1.5 hours, will be held in a private room at the FACES clinic, and will be recorded with a digital voice recorder.
The interviews will follow a semi-structured format, with probing for key components reflected in our conceptual framework. For example, the first interview will probe for engagement in preparations for newborn care, infant feeding intentions, how a newborn will impact engagement in HIV treatment, anticipated family support, access to and quality of food, factors causing anxiety, perceptions of mental health and its impact on engagement in care. Subsequent interviews will focus on key mental health and FI issues associated with each time point and tailored to assessing our framework. Based on the iterative nature of longitudinal qualitative interviews, the content of the 2nd, 3rd, and 4th interviews will be based on findings from the first interview. When possible, one interviewer will complete all interviews to build rapport and to aid in retention

For a number of reasons, there is no feasible remote option to carry out our in-depth interviews. We need face to face interactions to elicit in depth responses to our interview questions by ensuring participant privacy and comfort. We also need to capture non-verbal cues and body language as they are important components which guide our use of interview probes. Given our participants do not have access to good reliable internet/phone we would not be able to effectively and securely capture audio or video interviews remotely. Therefore, taking into consideration current public health guidelines to reduce COVID-19 exposure (as outlined in the KEMRI SERU Guidelines for the Conduct of Research During the COVID-19 Pandemic in Kenya), we will minimize the risk of exposure for research staff and participants by instituting the following procedures for our 4th and final in-depth interviews:

1) We will remotely screen participants for respiratory illness. Anyone who screens positive for exposure or suggestive symptoms will not be invited to the interview until COVID-19 has been ruled out and they will be referred to the Ministry of Health (MOH) for follow-up.
2) We will screen our staff daily for COVID-19 exposure and symptoms. Only staff without exposure or suggestive symptoms will conduct interviews with participants. Staff will also be encouraged to undergo free testing provided by the MOH.
3) At the interview site, we will implement all infection control measures as outline in the KEMRI SERU Guidelines for the Conduct of Research During the COVID-19 Pandemic in Kenya including: temperature checks, hand washing/ hand sanitizers for all to use, providing 3-ply faces masks to participants and staff and maintaining the recommended 1.5 meter distancing in a well ventilated spacious room.
4) We will train all staff on appropriate infection prevention measures to mitigate COVID-19 spread.

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(ii) Provisions for data verification and validation in the field and laboratory: All interviews will be transcribed and then translated into English. Audio files will promptly be deleted after the transcription is complete. Translations of the interviews and observational field notes will be analyzed using dedoose, a qualitative management program.

Phase Two (Intervention Development and Testing):

Intervention Development:

1. Key Informant Interviews

(a) Study site (geographical): The proposed study will be conducted in Kisumu county in the former Nyanza Region in western Kenya.

(b) Study populations: Self-described stakeholders in the health of perinatal women living with HIV such as those involved in providing healthcare and other resources to the women as well as those involved in creating policies and procedures that impact this population. For example, FACES clinic staff and mentor mothers who work directly with pregnant and postpartum women living with HIV.

(i)Inclusion criteria: Self-described key stakeholder in the health of perinatal women living with HIV and or experience working with pregnant and postpartum women living with HIV.

(ii)Exclusion criteria: Unwillingness or inability to participate.

(c) Sampling

(i) Sample size determination: Sample size determinations are based on standardized feasibility procedures outlined in the literature.[78-80]

(ii) Sampling procedures: 5-12 Key informants will be identified and selected by the PI an and Site Co-I. The sample will include a purposeful sample of key stakeholders identified by the PI and her mentors to ensure a variety of perspectives. Potential participants will be called by the site PI. They will be asked to participate in the evaluation

of the conceptual model and/or intervention. If they are interested, and available, the PI will set up a time for the interview to take place virtually through video/phone call and verbal consent will be obtained remotely.

(d) Procedures:

(i) Description of the type of data to be collected and collection procedures: Once a candidate intervention has been identified, preliminary research on its acceptability will be conducted. Key stakeholders will be individually presented with the intervention and asked questions about the intervention. The interview will last around 1.5 hours for each key informant and they will be asked to find a secure and private location with good network as the sessions will take place virtually through a video or phone call as convenient to the key informant. The purpose of the interview will be to gain insight as to the stakeholder's evaluation of the acceptability of the intervention. An interview guide for Key Informant interviews will be submitted with future amendments. Notes will be taken during the key informant interviews.

(ii) Provisions for data verification and validation in the field and laboratory: Most Key Informant interviews will be conducted in English. However, if necessary, the interviews will be recorded, transcribed and translated into English. If audio files are created, they will be promptly deleted after the audio is transcribed. Given our aim is to get feedback on the intervention, there is no need to record or transcribe interviews conducted in English for the purpose of analysis or publication.

2. Focus Group Discussions

(a) Study site (geographical): The proposed study will be conducted in Kisumu County in the former Nyanza Region in western Kenya.

(b) Study populations: (1-2 discussions with N=8-12 participants each) Postpartum women over 18 years of age.

(i)Inclusion criteria: a) 18 years or older, b) postpartum within 6 months of delivery c) HIV positive status based on clinic records, d) currently prescribed ART.

(ii)Exclusion criteria: a) self-reported participation in another ART adherence related study, or b) unable to understand consent process.

(c) Sampling

(i) Sample size determination: Sample size determinations are based on standardized feasibility procedures outlined in the literature.[78-80]

(ii) Sampling procedures: We will recruit 8-12 women for each discussion (up to 2 discussions) through designated FACES clinics in-person with a FACES staff member positioned in the clinic waiting room. Interested women will be assessed for eligibility using a brief screening assessment administered by a female study staff member. We will use purposeful sampling to ensure a diverse sample across ages, parity (1st pregnancy or subsequent pregnancies), and employment (employed vs. unemployed) Screening will be done

(d) Procedures

(i) Description of the type of data to be collected and collection procedures: The focus group discussion will be held in a private room at the FACES clinic and last approximately 1-2 hours. Participants will be asked maintain the confidentiality of their fellow participants and not to disclose any information discussed within the group. The group will be presented with an overview of the intervention and asked for feedback. The moderator will probe for feedback on acceptability of content, delivery of content and design. Provided all participants consent to being recorded, focus groups discussions will be audio recorded for qualitative analysis purposes. If any participants do not wish to be recorded, the discussions will not be recorded and detailed notes will be taken. Recordings will be transcribed and audio files promptly deleted after the transcription is complete. No identifying information will be revealed in the transcripts (transcribers will be instructed to remove any identifying information, and replace first names with generic terms, such as female 1, female 2, etc.). Participants' names will not be linked to this data in any way.

(ii) Provisions for data verification and validation in the field and laboratory: All focus group transcriptions will be transcribed and translated into English. The translations and observational field notes will be analyzed using dedoose, a qualitative management program.

Intervention Pilot Test

(a) Study site (geographical): The proposed study will be conducted in Kisumu County in the former Nyanza Region in western Kenya.

(b) Study populations: Pregnant and postpartum women over 18 years of age.

(i)Inclusion criteria: a) 20-35 weeks pregnant, b) Living with HIV, c) currently prescribed ART.

(ii)Exclusion criteria: a) High-risk pregnancy for reasons other than HIV status (e.g., pregnancy complications, preeclampia, gestational diabetes, preterm labor), b) Self-reported participation in another ART adherence-related intervention study, c) Unable to understand consent process, and d) Planning on relocating out of Nyanza province in the following 12 months.

(c) Sampling

(i) Sample size determination: Sample size determinations are based on standardized feasibility procedures outlined in the literature.[78-80]

(ii) Sampling procedures: We will recruit 40 pregnant women from 2 designated clinics. 20 women will be recruited from Lumumba sub-County Hospital to participate in our intervention. During the same period, 20 women will be recruited from Kisumu County Hospital to participate as our control group. We have opted to use an alternate clinic site for the control group not receiving cash transfers to avoid interactions between women receiving cash transfers and women not receiving cash. We will recruit in-person, with a clinic staff member positioned in the clinic waiting room. Interested women will be assessed for eligibility using a brief screening assessment administered by a female study staff member. For women who are eligible, the staff member will privately give a more complete description of the study, and if the individual is interested, the consent process will begin.

(d) Procedures

(i) Description of the intervention pilot test: To test feasibility, we will recruit and enroll N= 40 women, 20-35 weeks pregnant, 18-years and above, living with HIV (n=20 for the intervention group and n=20 for the control group).

Intervention group (n=20): Women in the intervention group will receive personalized support for breastfeeding provided by a local skilled lactation specialist and a monthly UCT of 10,000KES.

Women in this arm of the study will meet with a lactation consultant at 5 timepoints throughout the intervention: once during pregnancy and at 2-weeks, 4-weeks, 6-weeks and 3-months postpartum. During pregnancy, the lactation specialist will assess women's knowledge and experience with regards to breastfeeding and provide them information and support for optimal infant feeding after birth while emphasizing exclusive breastfeeding. Each post-partum visit with the lactation specialist will be individualized and continue to focus on optimizing infant feeding with a focus on exclusive breastfeeding for up to 6-months postpartum. During the postpartum sessions, the lactation specialist will assess for milk sufficiency or any other barriers to optimal infant feeding. The assessment will include the infant's weight and a physical assessment of women's breasts and breastfeeding practice. The lactation specialist will counsel women on how to address both perceived and actual milk insufficiency as well as address any of the other barriers to infant feeding as appropriate. Counseling topics will include women's breastfeeding timing and technique, diet, hydration and infant hunger and satiety cues to optimize safe infant feeding. Other treatments may include warm or cold compresses or the use of a breast pump to treat engorged breasts. The lactation specialist will not prescribe women any medications. Any medications the lactations specialist would recommend (for example an antibiotic to treat mastitis) will be recommended to the participant's primary perinatal care provider for further consideration and prescribing as appropriate. At the last visit (3-months postpartum) the lactation specialist will provide women with support and information about when and how to introduce affordable nutritious supplemental foods to their infants while at the same time promoting continued breastfeeding for 24-months or beyond.

Women in the intervention group will also receive monthly UCT of 10,000KES sent directly to an MPESA accounts associated with their personal cell phone. Cash transfers using MPESA accounts have an electronic trail for auditing purposes and such transactions have already been successfully used in healthcare research in Kenya.[92] If any interested and eligible participant does not have their own cellular phone with MPESA account, they will be provided with a low-cost phone for use during the study period. As a University of California San Francisco affiliated study, our research team will work together with the finance team at Global Programs Kenya to administer the UCT to participants.

Control Group (n=20): The women enrolled in the control arm will receive standard care. After the last data collection for the control group is complete (at around 6-months postpartum), control group participants will be offered a one-on-one informational session, designed by a lactation specialist, and provided by the same RA who administered the electronic surveys throughout the study period. The session will provide women with support and information about how to introduce affordable, nutritious supplemental foods to their infants while at the same time promoting continued breastfeeding for 24-months or beyond. The session will last 20-40 minutes, depending on the number of questions participants have.

(ii) Description of the type of data to be collected and collection procedures: Participants in both the intervention and control groups will be asked to complete electronic surveys via tablet at baseline (20-35 weeks pregnant), 2-weeks, 4-weeks, 6-weeks, 3-months and 6-months. The electronic surveys will collect information on a variety of outcomes including socio-demographics, FI, financial stability, mental health, infant health, relationships, stigma, empowerment, breastfeeding practices and adherence to HIV medications for participants and their infants (see Table 3 for all topics and specific tools to be included in the survey). At each research encounter where the surveys will be completed, infants will also be weighed by a trained member of our research team and clinic records will be used to collect participant's viral loads, infants' HIV test results and information on health status and engagement in care for the participant and her infant (see also Table 3). At each research encounter, participants in both the intervention and control groups will be reimbursed for their transportation costs and provided with refreshments.

For participants in the intervention group, the lactation specialist will coordinate to meet women, whenever possible, on the same day of their research encounters with our Research Associate who will collect survey data and infant weights. To the extent possible, we will also arrange the research encounters to coincide with participants regular clinic visits. Following each session with participants, the lactation specialist will write or dictate a summary note to include her professional assessment with regards to the adequacy of the participants milk supply, her assessment of the woman's breastfeeding practices (i.e. to what extent women are exclusively breastfeeding and/or any successes or challenges women experience), and a summary of the counseling or treatment she provided.

Women from the intervention group will also be asked to participate in exit interviews, conducted at around 6-months postpartum, to assess the acceptability of all intervention components and to seek suggestions for improvement. An interview guide for the follow up interviews has been submitted for IRB approval along with this updated protocol.

Table 3

	Baseline: recruitment	Birth: no face-to-face encounter	2-weeks	4-weeks	6-weeks	3-months	6-months
Demographic and Individual item Questions							
Baseline questionnaire	x						
Breastfeeding focused follow-up questionnaire			x	x		x	
6-week follow-up questionnaire					x		
6-month follow-up questionnaire V 1.1							x
SCALES							
Mental Health: PHQ-9; Perceived stress scale	x				x		x
Food Insecurity: Household food insecurity access scale	x				x		x
Financial status: Wealth Index	x				x		x
Relationships: Couples Satisfaction Index	x				x		x
Breastfeeding: Prenatal BF Self-Efficacy (pre) Postpartum Breastfeeding Self Efficacy (PP)	X(pre)		X (PP)	X (PP)	X (PP)	X (PP)	X (PP)
Social support: The Duke-UNC Functional Social Support (DUFSSQ)	x				x		x
Empowerment: Demographic Health Survey Household decision making and IPV	x				x		x
HIV related stigma: 12-item HIV stigma scale	x				x		x
Infant weight measured by RAs			x	x	x	x	x
From participant's clinical record: hemoglobin, Viral Load	x					x	x
From infant's clinical record: # weeks gestation at birth, weight, length, HIV test results, vaccinations status		x	x		x	x	x
Qualitative Exit Interview Intervention Group Only							x

(ii) Provisions for data verification and validation in the field and laboratory: Our female RAs on site will ensure participants are able to read and understand survey questions. They will read the questions out loud to participants as needed and clarify the intended meaning of the questions without leading participants in any way and (to the extent possible) without viewing participants responses. The RAs will ensure all questions are answered unless intentionally skipped by participants. The RAs will then download and quality check the survey data to REDCap after each research encounter. The interviews conducted at the endpoint of the intervention will be transcribed and translated into English and quality checked by our experienced RAs. All recordings will be promptly deleted after transcription. Translated interviews and clinical notes from the lactation specialist will be analyzed using dedoose, a qualitative management program.

9. DATA MANAGEMENT

a) Data Storage

i. Provision for database management: Data from the tablets will be uploaded after each research encounter to a UCSF-based server. All records will be kept on password protected tablet computers. All participant record forms will be kept in individual files in a secured filing cabinet in an access-limited room at the health facility. Participant names and addresses will be stripped from the database prior to analysis. Audio files will not be downloaded from our secure server. They will be accessed directly from the server and once the transcription of the interview has been completed and verified, the audio files will be deleted. The responsible financial administrators at Global Program Kenya who will administer the UCTs will be properly trained on how to securely handle participants personal identifiable information (names and associated phone numbers). They will also receive CITI training. Such information will be maintained and communicated to only those with a need to know through UCSFs secure database.

ii. Description of devices to be used for storage: Data collected for this study will be entered into handheld computer tablets operating the Redcap system used by UCSF. The database will be protected by a separate password on password-protected tablets. Qualitative data and any electronic research documents will be stored in UCSF's secure database, "BOX."

(b) Data Management

i. Data analysis:

Phase One: The focus of this analysis is to connect themes both between participants, to gain an understanding of common experiences, and within participants across time, to better understand how FI and perinatal depression conditions change over time and those impacts on adherence to PMTCT outcomes. We will use grounded theory [69] and 'sensitizing concepts'[70] to guide analysis. Sensitizing concepts starts with a general reference point to guide interpretation of emerging themes while maintaining use of inductive analysis, a key principle of a grounded theory approach. Thus, we're able to guide our analysis from our conceptual framework while allowing for codes/themes to emerge from the data to yield a comprehensive picture of women's experiences. Constant comparative method will be used where each line, phrase, sentence and paragraph from interviews are reviewed to find concepts and code the data [69,71]. Reliability will be measured as the amount of inter-rater agreement using Cohen's Kappa, which measures agreement corrected for change. Discrepancies between coders will be discussed and resolved until >80% agreement in codes.

Phase Two: The key informant interviews and focus group discussions will provide us with feedback on a proposed intervention. Thus, data collected from these activities will be qualitatively reviewed and used to make modifications to the intervention before pilot testing. Content analysis[81] for the focus group discussions will be applied to coding and analysis using dedoose software. The focus of the analysis for the data collected during pilot testing will be to assess the impact of the intervention on measures such as depression, financial security, relationships, stress, empowerment, social support and adherence to PMTCT guidelines as well as to gather feedback from the women who participated in the intervention. Published scales will be scored according to the scales' guidelines. Although our sample size may be too small to detect statistically significant differences, we will use statistical analysis to look for difference/trends in scores across time within each group (intervention and control), as well as differences between the intervention and control group scores at each timepoint. After the pilot is complete, we will conduct exit interviews with participants in the intervention group to assess the acceptability of all intervention components and suggestions for improvement. Transcripts from these interviews will be coded and content analysis[81] will be used to group and summarize women's feedback regarding the intervention. Documentation from the lactation specialist will be analyzed using a longitudinal qualitative approach to determine the specific barriers or successes women experienced with regards to optimal infant feeding across time. The analysis will also identify what information, support or treatments were offered and to what extent women were able to overcome these barriers given the personalized care provided.

10. TIME FRAME/DURATION OF THE PROJECT:

	Year1		Year 2		Year 3		Year 4		Year 5	
Months	1-6	6-12	1-6	6-12	1-6	6-12	1-6	6-12	1-6	6-12
Operationalize study procedures										
Hire & train researchers										
Recruit participants and data collection Phase 1										
Process data from Phase 1										
Intervention development										
Recruit key informants/ focus group participants and initial data collection for Phase 2										
Revise and finalize intervention										
Phase 2 Pilot test of the intervention										
Process data from Phase 2										

11. ETHICAL CONSIDERATIONS

The study protocol and forms will be submitted to the UCSF Committee on Human Research, as well as the Scientific and Ethical Review Unit (SERU) of the Kenya Medical Research Institute (KEMRI). No aspect of the study will be conducted without explicit study approval from both UCSF CHR And KEMRI SERU.

(a) Human Subjects

(a1) "First, do no harm."

The primary risks associated with the study are loss of confidentiality and risks to reputation. Participation in this research and research results will be kept as confidential as possible. No individual identities will be used in any reports or publications resulting from the study.

There is also the risk of fatigue from interviewing or participation in the group discussion. In addition, participants will be asked some sensitive questions regarding mental health, which may lead to personal discomfort or embarrassment. Participants are free to decline to answer any questions and can stop the interview or leave the discussion at any time. Field staff will be trained in non-judgmental interactions, how to recognize and respond to any distress and strategies designed to minimize these risks and their potential impact on study participants. To avoid fatigue, interviews and discussions will be kept to no more than 2 hours, with breaks available as needed.

All serious and unexpected adverse events will be reported to the Study PIs and to the relevant IRBs per local regulation. We have preemptively come up with a number of procedures to protect study participants against any potential risks that may result from study participation, including:

Planned procedures for protecting against fatigue: Interviews as well as focus group discussions will last 1-2 hours. Participants will be informed that they can take a break or stop at any time. Staff will be well-trained and supervised under the direction of experienced clinical researchers.

Planned procedure for protection of risks due to sensitive questions: Efforts will be made to minimize discomfort by assuring that interviewers and discussion moderators are well trained and that they will inform participants beforehand about the nature of the questions and assure participants of privacy.

For the In-Depth Interviews: The interviewer will be available after the interview to debrief the participant if s/he is in any way concerned by the nature of the questions. Routine demographic questions will be asked first, followed by more personal questions. Participants will be informed that they have the right to decline participation in the study, to refuse to answer any questions, or to withdraw at any time without adverse consequences. Sensitive questions such as sexual risk may be asked using ACASI. Since the Ministry of Health with additional support from implementing partners such as the FACES program provides comprehensive AIDS education, counseling, and services, it will be possible for the interviewers to provide immediate referrals for research participants who are in emotional distress or exhibit any concerning physical signs or symptoms. As we will screen for depression, for participants who have suicidal thoughts, we will ask participants to speak with one of our study health providers who can further screen them for suicidal ideation and make appropriate referrals if they are suicidal. This may lead to some discomfort, but we hope will provide benefits for the participants if they are able to get access to appropriate mental health care.

For the Focus Group Discussions: **Disclosure of HIV status to other focus group participants by virtue of participating in the group.** Potential negative effects associated with this risk are minimized through our IRB-approved recruitment procedures and informed consent that clearly conveys to individuals that they will be identified as being HIV positive through participation in the focus group. Participants are informed of this risk, however cannot be fully protected from it. However, women attending PMTCT care are already unofficially disclosing their status by virtue of PMTCT counseling addressing HIV positive women. This does not lessen the impact of the potential risk, however, it speaks to women attending PMTCT are in essence self-disclosing to their peers already.

Potential for others in focus group to fail in maintaining participant's privacy. We cannot guarantee everyone will honor the pledge of confidentiality and therefore this is a risk that participants will be fully informed of during the IRB-approved recruitment procedures. To mitigate this risk, focus group facilitators will reinforce to participants to refrain from sharing something they feel uncomfortable with others hearing. Participants will also be reminded that part of participating in focus groups is the agreement that information shared within the group is confidential and not to be spoken of outside the group. If a participant does not feel she can maintain that agreement she will be asked not to participate.

For the Intervention Pilot Test: The lactation specialist who will be providing personalized lactation support will be trained on the protection of human subjects including maintaining privacy and handling personally identifiable information. The financial administrators facilitating the UCTs will also be trained and they will only be given the information about participants necessary for administering the monthly UCTs. A potential risk of the cash transfer is women could experience negative feelings including stress, anxiety or sadness if they are asked to or forced to share some or all of the money with their partners or others in their household/ community. We will assure women that no information about the monthly UCTs will be disclosed to anyone outside our study team. In addition, if women do not have access to a telephone of their own, we will provide them with a telephone for use to ensure to the extent possible the money will be privately and directly available to them. We will also monitor closely including via monthly follow-up phone calls with participants to promptly identify and address any adverse events experienced by women related to the monthly UCTs. Cash transfers have been used widely in a variety of settings to include similar sums of money without negative consequences to recipients. We will also discuss the progress of our study regularly with clinic staff at our research sites to identify any real or potential negative impact related to the intervention. To reduce risk of any negative interaction between our intervention and control arms we will be using two separate, but matched, clinics. In this way we attempt to avoid a potential situation where women in the control group discuss their participation in the study with women in the intervention group and vice versa leading to the control group to feel negatively about the study or members of the intervention group as they are not receiving the same supportive intervention.

Planned procedure for reporting of adverse events: All serious adverse events associated with the procedures of this study will be reported within 10 days to the appropriate IRBs. Current guidance on adverse event reporting has focused on clinical trials of drugs or devices and has not provided clear guidance on behavioral prevention trials. The primary risk to subjects in this study is loss of confidentiality. If serious or unexpected adverse events occur, these will be filed with the appropriate IRBs within ten working days. We will ask study participants to return to the research field site in the case of ongoing adverse events. We will also provide participants with a palm card containing information on how to contact the local field staff to report such incidents as HIV-related disruption of families, acts of discrimination, physical harm, adverse events following phlebotomy, or personal distress. Field staff will be trained to complete descriptions of adverse events that will then be sent electronically to the study PIs.

(a2) Potential benefits of the proposed research to the subjects and others

Participants in the study will be able to access the results of the study. The research findings have the potential to ultimately benefit other perinatal women in Kenya and elsewhere is sub-Saharan Africa who are struggling with the overlapping epidemics of food insecurity, mental health and HIV. In view of the minimal risks to subjects, and the many actual and anticipated potential benefits to research subjects and others in their community, we believe that the benefits strongly outweigh the risks. The receipt of unconditional cash transfers may provide considerable benefit to participants in meeting basic needs for themselves and their dependents during a period of time while perinatal women are typically out of the workforce. In addition, the lactation support may have direct and immediate benefit to breastfeeding women who are also confronting food insecurity, breast health concerns and other complexities that may challenge their ability to exclusively breastfeed.

The research will not provide any direct benefits to the participants, other than possible psychological benefits associated with sharing their insights and stories. As a token of appreciation, participants in the in-depth interviews and focus group discussions will be compensated for their time with up to 800 Kenyan Shillings (equivalent to ~$8) per interview or group discussion.

(a3) Informed Consent

Research will be conducted according to Good Clinical Practice guidelines, the U.S. Code of Federal Regulations (CFR) Title 21 CFR (Part 50 – Protection of Human Subjects and Part 56 – Institutional Review Boards), and the Declaration of Helsinki. This protocol has been approved by UCSF's Committee on Human Research (letter attached). The informed consent of each participant will be obtained before protocol-specified procedures are carried out.

The consent process will be conducted with a staff member fluent in English, Swahili and Dholou who has been trained in research ethics and the specific consenting protocol for this study. The consent process will be conducted in the language of the participants choosing. The informed consent process will highlight the specific risks associated with the study, including discomfort from in-depth discussions of HIV infection, perinatal depression and mother-to-

child transmission of HIV and risks for breaches to confidentiality. The participants will be informed about the precautions put in place to minimize the risk of breaches in confidentiality. The participants will be informed about all procedures put in place to reduce the risk of breaches in confidentiality including: the use of a unique participant ID number on all research data and that her name will not be used in relation to her data and that all data will be kept in a safe, locked filing cabinet or password-protected computer in a locked office. It will also be noted that study staff are not practicing doctors, nurses or any type of healthcare provider and, thus, cannot diagnose, treat or prescribe medications of any kind. The participant will be allowed to ask questions and the staff member will probe for complete understanding during key points of the consent form. The participant can take as much time as they need to make a decision and she will be reminded that she can de-enroll in the study at any time and that participation is completely voluntary and will not impact her regular clinic visits. All participants will be provided the contact numbers of the PI Dr. Tuthill, Dr. Bukusi and the KEMRI IRB chairs to answer any questions that the participant might have about the study or one's rights as a human subject. Completed, signed consent forms will be kept in a locked filing cabinet in our secured research office. The participant will be allowed to take a copy of the consent form home to have a reference, but will be reminded that someone finding the form may result in a breach of confidentiality.

We have developed a separate informed consent for intervention and control participants based on previously established protocols for conducting research when an intervention involves cash transfers. This will ensure the participants in each arm are not influenced by the other. Given cash transfers need to be handled with care because they provide financial assistance to a vulnerable population these additional steps are critical for protecting human subjects.

(a4) Method of maintaining confidentiality of information obtained during the study:

To ensure confidentiality of participation, all data will be coded by a unique participant identifier number. Data will be kept in locked cabinets and will only be provided to a subject's clinician upon the written request of the subject. Research records will be kept confidential to the level allowed by law. For interview data, survey data and any participant data recorded by our lactation specialist collected as part of the study, subjects will be assigned a unique study identification number. Interviewers and support staff including the lactation specialist and financial administrator assisting with cash transfers will be trained on procedures for maintaining privacy and will sign a pledge of confidentiality. Additionally, discussion group participants will be asked to pledge that they will not share the personal information of others, disclosed in the session, with anyone outside of the group. All transcripts and computer records will be password-protected to prohibit illicit access. All personal identifiers will be removed from any paper or electronic study forms, which will be coded only by numerical identifiers. When these procedures are followed, it is highly unlikely that any information revealed by participants during the course of the interviews or clinic visits will be disclosed to anyone outside the research team.

Primary responsibility for data and safety monitoring will fall on the PIs (Drs. Tuthill and Bukusi). In this research, the primary risk to subjects is loss of confidentiality. Risks to participants will be minimized through informed consent and strict confidentiality. In the case of any serious adverse events, we will ask subjects to return to the research field site. We will also provide subjects with an informed consent translated into the local language of their choice, so that they have the opportunity to contact the local field staff or one of the study investigators at any time. Study staff will be trained to complete descriptions of adverse events that will be sent electronically to the principal investigators (Drs. Tuthill and Bukusi). Serious or unexpected AEs will be reported to the appropriate IRBs within 10 working days of awareness of the incident.

(a5) Not applicable.

(b) Animal subjects

Not applicable.

12. EXPECTED APPLICATION OF RESULTS

This study will fill key gaps about the interplay of FI and perinatal depression and its impact on adherence to PMTCT strategies among women living with HIV, specifically during the transition period from pregnancy to postpartum. Background literature suggests there is causal, additive impact between FI and perinatal depression on ART adherence and exclusive breastfeeding, however, how impactful this relationship may be and at what point during the perinatal period these factors are most detrimental is not known. Furthermore, both FI and perinatal depression are substantial maternal and infant health issues in their own right. Addressing them together through a multi-level intervention designed to promote adherence to PMTCT strategies will have the added benefit of improving overall health.

These efforts are aimed to help impact Sustainable Development Goals: 1) improve maternal and infant health and 2) further several top Sustainable Development Goals (SDG) including SDG 1 (zero poverty), SDG 2 (zero hunger), SDG 3 (good health and wellbeing), and SDG 5 (gender equality).

13. References

1. UNAIDS. GLOBAL AIDS UP DATE 2016. June 2016:1-16.

2. Johansson K, Robberstad B, Norheim O. Further benefits by early start of HIV treatment in low income countries: Survival estimates of early versus deferred antiretroviral therapy. *AIDS Research & Therapy*. 2010;7(1):3-9. doi:10.1186/1742-6405-7-3.

3. The INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. *The New England journal of medicine*. 2015;373(9):795-807. doi:10.1056/NEJMoa1506816.

4. Gopalappa C, Stover J, Shaffer N, Mahy M. The costs and benefits of Option B+ for the prevention of mother-to-child transmission of HIV. *AIDS*. 2014;28:S5-S14. doi:10.1097/QAD.0000000000000083.

5. Ciaranello AL, Perez F, Engelsmann B, et al. Cost-effectiveness of World Health Organization 2010 Guidelines for Prevention of Mother-to-Child HIV Transmission in Zimbabwe. *Clinical Infectious Diseases*. 2012;56(3):430-446. doi:10.1093/cid/cis858.

6. Fasawe O, Avila C, Shaffer N, et al. Cost-Effectiveness Analysis of Option B for HIV Prevention and Treatment of Mothers and Children in Malawi. *PloS one*. 2013;8(3):e57778. doi:10.1371/journal.pone.0057778.

7. Coutsoudis A, Goga A, Desmond C, Barron P, Black V, Coovadia H. Is Option B+ the best choice? *Lancet*. 2013;381(9863):269-271. doi:10.1016/S0140-6736(12)61807-8.

8. Sherr K, Gimbel S, Rustagi A, et al. Systems analysis and improvement to optimize pMTCT (SAIA): a cluster randomized trial. *Implement Sci*. 2014;9(1):55. doi:10.1186/1748-5908-9-55.

9. Plessis du E, Shaw SY, Gichuhi M, et al. Prevention of mother-to-child transmission of HIV in Kenya: challenges to implementation. *BMC health services research*. 2014;14(Suppl 1):S10. doi:10.1186/1472-6963-14-S1-S10.

10. Manzi M, Zachariah R, Teck R, et al. High acceptability of voluntary counselling and HIV-testing but unacceptable loss to follow up in a prevention of mother-to-child HIV transmission programme in rural Malawi: scaling-up requires a different way of acting. *Tropical medicine & international health : TM & IH*. 2005;10(12):1242-1250. doi:10.1111/j.1365-3156.2005.01526.x.

11. Psaros C, Remmert JE, Bangsberg DR, Safren SA, Smit JA. Adherence to HIV Care After Pregnancy Among Women in Sub-Saharan Africa: Falling Off the Cliff of the Treatment Cascade. *Current HIV/AIDS reports*. 2015;12(1):1-5. doi:10.1007/s11904-014-0252-6.

12. Kurewa EN, Kandawasvika GQ, Mhlanga F, et al. Realities and Challenges of a Five Year Follow Up of Mother and Child Pairs on a PMTCT Program in Zimbabwe. *Open AIDS J*. 2011;5(1):51-58. doi:10.2174/1874613601105010051.

13. Ogunbosi BO, Oladokun RE, Awolude O, et al. Missed Opportunities for Prevention of Mother-to-Child Transmission of HIV (PMTCT) in Ibadan, Southwest Nigeria. *WJA*. 2014;04(03):356-364. doi:10.4236/wja.2014.43042.

14. Coovadia HM, Rollins NC, Bland RM, et al. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. *Lancet*. 2007;369(9567):1107-1116. http://ac.els-cdn.com/S0140673607602839/1-s2.0-S0140673607602839-main.pdf?_tid=9f88124c-22af-11e2-9c6b-00000aab0f6c&acdnat=1351615026_3737425133192e43ce2b76e99fc5a57c.

15. dyj. Kenya AIDS Response Progress Report 2014 Progress towards Zero March 2014. July 2014:1-41.

16. Minniear TD, Girde S, Angira F, et al. Outcomes in a Cohort of Women Who Discontinued Maternal Triple-Antiretroviral Regimens Initially Used to Prevent Mother-to-Child Transmission during Pregnancy and

Breastfeeding—Kenya, 2003–2009. Newell M-L, ed. *PloS one*. 2014;9(4):e93556–5. doi:10.1371/journal.pone.0093556.

17. Nachega JB, Uthman OA, Anderson J, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries. *AIDS*. 2012;26(16):2039-2052. doi:10.1097/QAD.0b013e328359590f.

18. Hansen K. Breastfeeding: a smart investment in people and in economies. *The Lancet*. 2016;387(10017):416. doi:10.1016/S0140-6736(16)00012-X.

19. FILCA MHLMMIFF. Breastfeeding: Population-Based Perspectives. *Pediatric Clinics of NA*. 2013;60(1):11-30. doi:10.1016/j.pcl.2012.09.011.

20. Rollins NC, Bhandari N, Hajeebhoy N, Horton S. Why invest, and what it will take to improve breastfeeding practices? *The Lancet*. 2016;387(10017):491-504. doi:10.1016/S0140-6736(15)01044-2.

21. Karim QA, Banegura A, Cahn P, et al. Asking the right questions: developing evidence-based strategies for treating HIV in women and children. *BMC public health*. 2011;11(1):AbstractH–1230. doi:10.1186/1471-2458-11-388.

22. Weiser SD, Yuan C, Guzman D, et al. Food insecurity and HIV clinical outcomes in a longitudinal study of urban homeless and marginally housed HIV-infected individuals. *AIDS (London, England)*. 2013;27(18):2953-2958. doi:10.1097/01.aids.0000432538.70088.a3.

23. Kaaya S, Garcia ME, Li N, et al. Association of maternal depression and infant nutritional status among women living with HIV in Tanzania. *Maternal & Child Nutrition*. 2014;12(3):603-613. doi:10.1111/mcn.12154.

24. Weiser SD, Frongillo EA, Ragland K, Hogg RS, Riley ED, Bangsberg DR. Food Insecurity is Associated with Incomplete HIV RNA Suppression Among Homeless and Marginally Housed HIV-infected Individuals in San Francisco. *J GEN INTERN MED*. 2008;24(1):14-20. doi:10.1007/s11606-008-0824-5.

25. McCoy SI, Buzdugan R, Mushavi A, Mahomva A, Cowan FM, Padian NS. Food insecurity is a barrier to prevention of mother-to-child HIV transmission services in Zimbabwe: a cross-sectional study. *???* May 2015:1-9. doi:10.1186/s12889-015-1764-8.

26. Kalichman SC, Cherry C, Amaral C, et al. Health and Treatment Implications of Food Insufficiency among People Living with HIV/AIDS, Atlanta, Georgia. *J Urban Health*. 2010;87(4):631-641. doi:10.1007/s11524-010-9446-4.

27. Ivers LC, Cullen KA. Food insecurity: special considerations for women. *American Journal of Clinical Nutrition*. 2011;94(6):1740S–1744S. doi:10.3945/ajcn.111.012617.

28. Laraia BA, Siega-Riz AM, Gundersen C. Household Food Insecurity Is Associated with Self-Reported Pregravid Weight Status, Gestational Weight Gain, and Pregnancy Complications. *YJADA*. 2010;110(5):692-701. doi:10.1016/j.jada.2010.02.014.

29. Borders A, Grobman WA, Amsden LB. Chronic stress and low birth weight neonates in a low-income population of women. *Obstetrics and gynecology*. 2007;109(2 PART 1):331-338. doi:10.1097/01.AOG.0000250535.97920.b5.

30. Young SL, Mbuya MNN, Chantry CJ, et al. Current Knowledge and Future Research on Infant Feeding in the Context of HIV: Basic, Clinical, Behavioral, and Programmatic Perspectives. *Advances in Nutrition: An International Review Journal*. 2011;2(3):225-243. doi:10.3945/an.110.000224.

31. Zaslow M, Bronte-Tinkew J, Capps R, Horowitz A, Moore KA, Weinstein D. Food Security During Infancy: Implications for Attachment and Mental Proficiency in Toddlerhood. *Matern Child Health J*. 2008;13(1):66-80. doi:10.1007/s10995-008-0329-1.

32. Gillespie S, Kadiyala S. HIV/AIDS and food insecurity and nutrition: from evidence to action. May 2005:1-4.

33. Nanni MG, Caruso R, Mitchell AJ, Meggiolaro E, Grassi L. Depression in HIV Infected Patients: a Review. *Curr Psychiatry Rep*. 2014;17(1):e442.2006-e442.2011. doi:10.1007/s11920-014-0530-4.

34. Loftus H, Burnett A, Naylor S, Bates S, Greig J. HIV control in postpartum mothers: a turbulent time. *Int J STD AIDS*. 2016;27(8):680-683. doi:10.1177/0956462415601913.

35. Peltzer K, Rodriguez VJ, Jones D. Prevalence of prenatal depression and associated factors among HIV-positive women in primary care in Mpumalanga province, South Africa. *SAHARA J*. 2016;13(1):60-67. doi:10.1080/17290376.2016.1189847.

36. Zunner B, Dworkin SL, Neylan TC, et al. HIV, violence and women: Unmet mental health care needs. *Journal of Affective Disorders*. 2015;174:619-626. doi:10.1016/j.jad.2014.12.017.

37. Blashill AJ, Bedoya CA, Mayer KH, et al. Psychosocial Syndemics are Additively Associated with Worse ART Adherence in HIV-Infected Individuals. *AIDS & Behavior*. 2014;19(6):981-986. doi:10.1007/s10461-014-0925-6.

38. Hasselmann MH, Werneck GL, da Silva CVC. Symptoms of postpartum depression and early interruption of exclusive breastfeeding in the first two months of life. *Cadernos de Saúde Pública*. 2008;24(suppl 2):s341-s352. doi:10.1590/s0102-311x2008001400019.

39. Rahman A, Hafeez A, Bilal R, et al. The impact of perinatal depression on exclusive breastfeeding: a cohort study. *Maternal & Child Nutrition*. 2015;12(3):452-462. doi:10.1111/mcn.12170.

40. Ahlqvist-Björkroth S, Vaarno J, Junttila N, et al. Initiation and exclusivity of breastfeeding: association with mothers“ and fathers” prenatal and postnatal depression and marital distress. *Acta Obstet Gynecol Scand*. 2016;95(4):396-404. doi:10.1111/aogs.12857.

41. Aaron E, Bonacquisti A, Geller PA, Polansky M. Perinatal Depression and Anxiety in Women with and without Human Immunodeficiency Virus Infection. *Womens Health Issues*. 2015;25(5):579-585. doi:10.1016/j.whi.2015.04.003.

42. Yotebieng KA, Fokong K, Yotebieng M. Depression, retention in care, and uptake of PMTCT service in Kinshasa, the Democratic Republic of Congo: a prospective cohort. *AIDS Care*. 2016;29(3):285-289. doi:10.1080/09540121.2016.1255708.

43. Hernandez DC, Marshall A, Mineo C. Maternal Depression Mediates the Association Between Intimate Partner Violence and Food Insecurity. *J Womens Health (Larchmt)*. 2014;23(1):29-37. doi:10.1089/jwh.2012.4224.

44. Hadley C, Patil CL. Food insecurity in rural Tanzania is associated with maternal anxiety and depression. *Am J Hum Biol*. 2006;18(3):359-368. doi:10.1002/ajhb.20505.

45. Tsai AC, Bangsberg DR, Frongillo EA, et al. Food insecurity, depression and the modifying role of social support among people living with HIV/AIDS in rural Uganda. *Social Science & Medicine*. 2012;74(12):2012-2019. doi:10.1016/j.socscimed.2012.02.033.

46. Drake AL, Unger JA, Ronen K, et al. Evaluation of mHealth strategies to optimize adherence and efficacy of Option B+ prevention of mother-to-child HIV transmission: Rationale, design and methods of a 3-armed randomized controlled trial. *Contemporary Clinical Trials*. 2017;57:44-50. doi:10.1016/j.cct.2017.03.007.

47. Ashiono E, Achwoka D, Mutugi J, Rakwar J, Wafula A, Chabikuli ON. Vertical HIV transmission in perinatally-exposed infants in South-Rift region of Kenya: a retrospective cross sectional study. *BMC public health*. 2017;17(1):1-8. doi:10.1186/s12889-017-4124-z.

48. Ambia J, Mandala J. A systematic review of interventions to improve prevention of mother-to-child HIV transmission service delivery and promote retention. *Journal of the International AIDS Society*. 2016;19(1):1-11. doi:10.7448/IAS.19.1.20309.

49. Psaros C, Remmert JE, Bangsberg DR, Safren SA, Smit JA. Adherence to HIV Care After Pregnancy Among Women in Sub-Saharan Africa: Falling Off the Cliff of the Treatment Cascade. *Current HIV/AIDS reports*. 2015;12(1):1-5. doi:10.1007/s11904-014-0252-6.

50. Fayorsey RN, Chege D, Wang C, Reidy W. Mother Infant Retention for Health (MIR4Health): Study Design, Adaptations, and Challenges With PMTCT Implementation Science Research. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology*. 2016;72:S137-S144. doi:10.1097/QAI.0000000000001060.

51. Eide KT, Fadnes LT, Engebretsen IMS, et al. Impact of a peer-counseling intervention on breastfeeding practices in different socioeconomic strata: results from the equity analysis of the PROMISE-EBF trial in Uganda. *Global Health Action*. 2016;9(1):30578–10. doi:10.3402/gha.v9.30578.

52. Rotheram-Borus MJ, Richter L, Van Rooyen H, et al. A cluster randomised controlled trial of the community effectiveness of two interventions in rural Malawi to improve health care and to reduce maternal, newborn and infant mortality. *Trials*. 2010;11:88.

53. Tylleskär T, Jackson D, Meda N, et al. Exclusive breastfeeding promotion by peer counsellors in sub-Saharan Africa (PROMISE-EBF): a cluster-randomised trial. *Lancet*. 2011;378(9789):420-427. doi:10.1016/S0140-6736(11)60738-1.

54. Tuthill EL, Butler LM, Pellowski JA, McGrath JM. Exclusive breast-feeding promotion among HIV-infected women in South Africa: an Information–Motivation–Behavioural Skills model-based pilot intervention. *Public Health …*. 2017;20(08):1481-1490. doi:10.1017/S1368980016003657&domain=pdf.

55. Whittle HJ, Palar K, Seligman HK, Napoles T, Frongillo EA, Weiser SD. How food insecurity contributes to poor HIV health outcomes: Qualitative evidence from the San Francisco Bay Area. *Social Science & Medicine*. 2016;170(C):228-236. doi:10.1016/j.socscimed.2016.09.040.

56. Masa R, Chowa G. A Multilevel Conceptual Framework to Understand the Role of Food Insecurity on Antiretroviral Therapy Adherence in Low-Resource Settings: From Theory to Practice. *Social Work in Public Health*. 2017;00(00):1-15. doi:10.1080/19371918.2017.1289874.

57. Kaufman MR, Cornish F, Zimmerman RS. Health behavior change models for HIV prevention and AIDS care: practical recommendations for a multi-level approach. *Journal of acquired …*. 2014.

58. Rondon MB. Mental Health: At the Root of Human Development. *J Womens Health (Larchmt)*. 2014;23(1):1-2. doi:10.1089/jwh.2013.4661.

59. Banerjee A, Duflo E, Goldberg N, et al. A multifaceted program causes lasting progress for the very poor: Evidence from six countries. *Science*. 2015;348(6236):1260799-1260799. doi:10.1126/science.1260799.

60. Ivers LC, Chang Y, Gregory Jerome J, Freedberg KA. Food assistance is associated with improved body mass index, food security and attendance at clinic in an HIV program in central Haiti: a prospective observational cohort study. *AIDS Research & Therapy*. 2010;7(1):33-38. doi:10.1186/1742-6405-7-33.

61. Anema A, Vogenthaler N, Frongillo EA, Kadiyala S, Weiser SD. Food insecurity and HIV/AIDS: current knowledge, gaps, and research priorities. *Current HIV/AIDS reports*. 2009;6(4):224-231.

62. Weaver LJ, Hadley C. Moving Beyond Hunger and Nutrition: A Systematic Review of the Evidence Linking Food Insecurity and Mental Health in Developing Countries. *Ecology of Food and Nutrition*. 2009;48(4):263-284. doi:10.1080/03670240903001167.

63. Weiser SD, Young SL, Cohen CR, et al. Conceptual framework for understanding the bidirectional links between food insecurity and HIV/AIDS. *The American Journal of Clinical Nutrition*. 2011;94(6):1729S–1739S. doi:10.3945/ajcn.111.012070.

64. Singer M, Clair S. Syndemics and Public Health: Reconceptualizing Disease in Bio-Social Context. *Medical Anthropology Quarterly*. 2003;17(4):423-441. doi:10.1525/maq.2003.17.4.423.

65. Dennis CL, Faux S. Development and psychometric testing of the Breastfeeding Self-Efficacy Scale. *Res Nurs Health*. 1999;22(5):399-409. http://onlinelibrary.wiley.com.ezproxy.lib.uconn.edu/store/10.1002/(SICI)1098-240X(199910)22:5%3C399::AID-NUR6%3E3.0.CO;2-4/asset/6_ftp.pdf?v=1&t=h98zuoq4&s=52c3b89b5a1869586e28d12a186d15524636eed9.

66. Tsai AC, Bangsberg DR, Frongillo EA, et al. Food insecurity, depression and the modifying role of social support among people living with HIV/AIDS in rural Uganda. *Social Science & Medicine*. 2012;74(12):2012-2019. doi:10.1016/j.socscimed.2012.02.033.

67. Meffert SM, Neylan TC, Chambers DA, Verdeli H. Novel implementation research designs for scaling up global mental health care: overcoming translational challenges to address the world's leading cause of disability. *International Journal of Mental Health Systems*. 2016;10(1):1-6. doi:10.1186/s13033-016-0049-7.

68. Krippendorff K. *Content Analysis: an Introduction to Its Methodology*. 2012.

69. Glasser B. *Theorectical Sensitivity*. (Press S, ed.). 1978.

70. Bowen GA. Grounded theory and sensitizing concepts. *International Journal of Qualitative Methods*. 2006;5(3):12-23. doi:10.1177/160940690600500304.

71. Glasser B. *Basics of Grounded Theory Analysis*. (Press S, ed.). 1992.

72. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. *Journal of Psychiatric Research*. 2011;45(5):626-629. doi:10.1016/j.jpsychires.2010.10.008.

73. Moore CG, Carter RE, Nietert PJ, Stewart PW. Recommendations for Planning Pilot Studies in Clinical and Translational Research. *Clinical and Translational Science*. 2011;4(5):332-337. doi:10.1111/j.1752-8062.2011.00347.x.

75. Meleis, A. I. *Transitions Theory: Middle range and situation specific theories in research and practice.* New York, NY: Springer Publishing Company; 2010.

76. Meleis A. Transitions Theory. Penn Nursing. https://www.nursing.upenn.edu/live/files/552-transitions-theory. Accessed March 5, 2019.

77. Chick, N, Meleis, A. I. Transitions: A nursing concern. In Chinn P.L, ed. *Nursing research methodology: Issues and implementation.* Rockville, MD: Aspen; 1986: 237–257.

78. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. Journal of Psychiatric Research. 2011;45(5):626-629. doi:10.1016/j.jpsychires.2010.10.008.

79. Moore CG, Carter RE, Nietert PJ, Stewart PW. Recommendations for Planning Pilot Studies in Clinical and Translational Research. Clinical and Translational Science. 2011;4(5):332-337. doi:10.1111/j.1752-8062.2011.00347.x.

80. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. Journal of Evaluation in Clinical Practice. 2004;10(2):307-312. doi:10.1111/j..2002.384.doc.x.

81. Krippendorff K. Content Analysis: an Introduction to Its Methodology. 2012.

82. Tuthill, E.L., et al., *"I Found Out I was Pregnant, and I Started Feeling Stressed": A Longitudinal Qualitative Perspective of Mental Health Experiences Among Perinatal Women Living with HIV.* AIDS Behav, 2021.

83. Haushofer, J. and J. Shapiro, *The Short-Term Impact of Unconditional Cash Transfers to the Poor: Experimental Evidence from Kenya.* Q J Econ, 2016. **131**(4): p. 1973-2042.

84. Junior, J.K., Arlene M.; Ahn, Roy, *The Perspectives of Young Women in Rural Western Kenya on Unconditional Cash Transfers.* Poverty and Public Policy 2016.

85. Østergaard LR, Bula A. "They call our children „Nevirapine Babies?": A Qualitative Study about Exclusive Breastfeeding among HIV Positive Mothers in Malawi. *African journal of reproductive health.* 2010;14(3):213-222.

86. Operto E. Knowledge, attitudes, and practices regarding exclusive breastfeeding among HIV-positive mothers in Uganda: A qualitative study. *Int J Health Plann Manage.* Jul 2020;35(4):888-896.

87. Chikhungu LC, Bispo S, Rollins N, Siegfried N, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-infected women on antiretroviral treatment. *Tropical medicine & international health.* 2016;21(7):820-828.

88. Dunkley E, Ashaba S, Burns B, et al. "I beg you...breastfeed the baby, things changed": infant feeding experiences among Ugandan mothers living with HIV in the context of evolving guidelines to prevent postnatal transmission. *BMC Public Health.* Jan 29 2018;18(1):188.

89. Mohamed MJ, Ochola S, Owino VO. A Qualitative Exploration of the Determinants of Exclusive Breastfeeding (EBF) Practices in Wajir County, Kenya. *International breastfeeding journal.* 2020;15(1):44-44.

90. Duran MC, Bosire R, Beima-Sofie KM, et al. Women's Autonomy in Infant Feeding Decision-Making: A Qualitative Study in Nairobi, Kenya. *Matern Child Health J.* May 2021;25(5):724-730.

91. *Informal Sectors Skills and Occupations Survey (ISSOS): Basic Report*: Kenya Bureau of National Statistics 2020.

92. Wakadha, H., et al., *The feasibility of using mobile-phone based SMS reminders and conditional cash transfers to improve timely immunization in rural Kenya.* Vaccine, 2013. **31**(6): p. 987-993.