Development of a digital intervention to address stigma among pregnant unmarried adolescents living with HIV

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1. TITLE OF THE PROJECT:

Development of a digital intervention to address stigma among pregnant unmarried adolescents living with HIV

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Acronyms and Abbreviations

ALHIV	Adolescents living with HIV
ART	Antiretroviral therapy
Co-I	Co-investigator
Co-PI	Co-principal investigator
COVID-19	Coronavirus disease 2019
CV	Curriculum vitae
DSMP	Data and Safety Monitoring Plan
CSQ-8	8-item Client Satisfaction Questionnaire
DI	Dyadic interview
FGD	Focus group discussion
IDI	Individual in-depth interview
KEMRI	Kenya Medical Research Institute
MCH	Maternal and child health

mHealth	Mobile health
MTCT	Mother-to-child transmission
NASCOP	National AIDS and STI Control Programme
NIH	National Institutes of Health (USA)
PI	Principal investigator
PIRE	Pacific Institute for Research and Evaluation
PMTCT	Prevention of mother-to-child transmission of HIV
SCT	Social Cognitive Theory
SMS	Short Message Service (e.g.., text messaging)
SUS	System Usability Scale
U.S.	United States

3. ABSTRACT:

Kenya has high rates of mother-to-child transmission (MTCT) of HIV, large numbers of adolescents living with HIV (ALHIV), and elevated adolescent fertility rates. Stigma, undisclosed HIV status, and lack of social support may be key barriers to engagement in prevention of MTCT (PMTCT) services. Thus, addressing barriers to disclosure and social support may mitigate harmful effects of the intersecting stigmas of HIV and pregnancy on health outcomes. Growing evidence highlights the promise of digital interventions as important tools for improving HIV outcomes and communication with parents. However, digital interventions to address effects of stigma have not been explored among pregnant ALHIV. This study's specific aims are to: (1) Develop and evaluate a digital intervention for pregnant unmarried ALHIV aged 15-19 to increase awareness of stigma and its consequences; improve disclosure self-efficacy and skills; and facilitate enlistment of family caregivers as social support allies to enhance uptake of PMTCT services; and (2) Identify acceptable approaches to increase awareness about stigma and enhance skills in communication and provision of social support among family caregivers. We will use data from individual interviews with pregnant ALHIV and joint interviews with pregnant ALHIV/caregiver dyads to develop initial intervention specifications and mock-ups. We will conduct focus groups to obtain feedback on sample materials to develop an intervention prototype. We will then conduct a pilot to evaluate the prototype. We will conduct focus groups with caregivers to identify acceptable approaches to involve them. Data will be used to finalize content and specifications of the digital intervention for pregnant ALHIV and will provide the framework for a future intervention for caregivers, which will both be tested in a larger trial.

4. LAY SUMMARY:

Kenya is one of few countries that has a combination of high rates of mother-to-child transmission (MTCT) of HIV, large numbers of adolescents living with HIV (ALHIV), and elevated adolescent fertility rates. Kenya's comprehensive strategy to address MTCT includes HIV testing for all pregnant women, lifelong antiretroviral therapy (ART) for all pregnant women living with HIV, and counseling on HIV care, symptoms, linkage to treatment and support, and positive living. The strategy promotes at least four antenatal care (ANC) visits to obtain the necessary prevention of MTCT (PMTCT) services.

Pregnant ALHIV are less likely than adults to receive PMTCT services, thereby contributing to the high MTCT rate. Research among 15-19-year-old Kenyan ALHIV, including some who were pregnant, suggests that stigma, undisclosed HIV status, and lack of social support may be key barriers to engagement in HIV services, including PMTCT. Moreover, ALHIV often find out that they are HIV-infected and pregnant at the same time. Often, these adolescents delay disclosing their pregnancies and HIV status to parents due to fear of their reactions, which in turn delays engagement in ANC/PMTCT services.

Reducing barriers to disclosure and improving social support may lessen harmful effects of the intersecting stigmas of HIV and pregnancy on the health outcomes of pregnant ALHIV. Growing evidence highlights the promise smartphone-delivered digital interventions hold for facilitating HIV disclosure, improving treatment adherence among youth living with HIV, and preventing HIV and improving communication with parents among Kenyan youth. However, digital interventions to address the effects of stigma have not been explored among pregnant ALHIV.

We are conducting this study to (1) develop a smartphone-delivered digital intervention for pregnant unmarried ALHIV in Kenya and (2) identify acceptable approaches to improve the involvement of their caregiving family members. The goal of the digital intervention is to improve stigma awareness, disclosure of HIV and pregnancy, and social support to enhance adolescents' use of PMTCT services. We will answer the following questions in the study: (1) What are pregnant unmarried ALHIV's strategies for and experiences with disclosing their HIV and/or pregnancy status to their family caregivers? (2) What are pregnant unmarried ALHIV's strategies for and experiences with enlisting social support from their family caregivers? (3) What are pregnant unmarried ALHIV's experiences and strategies for coping with HIV and pregnancy stigma? and (4) What are acceptable approaches to increase awareness about stigma and improve skills in communication and provision of social support among family caregivers?

The study will take place in Kisumu and Siaya counties. It will involve about 198 participants who are pregnant, unmarried ALHIV (n=110) or caregivers of pregnant ALHIV (n=88). Depending on the study activity, we will select adolescents who have disclosed and not disclosed their pregnancy and/or HIV status to a caregiver. We will recruit participants from maternal and child health clinics in public health facilities in rural and urban sites. We will also use snowball sampling methods to recruit participants. Study participation will consist of one of the following activities (1) answer questions in an individual interview, (2) answer questions in a joint interview of a girl or young woman and her caregiver, (3) answer questions in a focus group discussion, or (4) test and evaluate a prototype digital intervention.

The risks of participation in the research are that (1) an ALHIV's HIV and/or pregnancy status could accidentally be revealed to family or community members and result in her experiencing stigma, and (2) a participant could feel emotional distress while participating in an interview because the topic of HIV and pregnancy are personal and sensitive. The benefits are that a participant may experience personal satisfaction from communicating with researchers about topics relevant to pregnant girls and young women living with HIV and being part of a study that could potentially help people in similar circumstances. The study will benefit society in that it will involve end users as partners in the development of a culturally-acceptable, feasible and effective digital intervention to lessen the harmful effects of stigma and enhance engagement in PMTCT services, thereby promoting the health of a vulnerable population of young mothers and their babies. The study will start on 1 February 2022 and finish on 31 May, 2023.

5. INTRODUCTION/BACKGROUND:

The Nyanza region in Kenya is a nexus for adolescent pregnancy and HIV infection. Kenya is among countries with the highest adolescent fertility rates (96 per 1,000 women aged 15-19 vs. 44 worldwide).[1-3] At 22% compared to 18% nationally, adolescent pregnancy is highest in Kenya's Nyanza region.[4,5] Kenya is also among four sub-Saharan African countries with the highest numbers of ALHIV aged 10-19 in the world.[6] In 2019, Kenyan females aged 15-24 comprised 110,000 persons living with HIV and 10,000 new infections.[6] Nyanza accounted for 41% of infected female youth and 46% of new

infections among female youth in the nation.[6] Nyanza counties most afflicted by HIV are Siaya, Kisumu, Migori, and Homa Bay.[7]

PMTCT engagement is sub-optimal among youth, leading to poor outcomes. Kenya is also among 7 countries that accounted for half of all new pediatric HIV infections in 2019.[6] MTCT incidence in the Nyanza counties most afflicted by HIV is 8-12%; they account for 34% of the nation's gap in PMTCT coverage.[7] Higher rates of MTCT to infants aged 4-8 weeks have been found among adolescent mothers (6.9%) compared to adult mothers (2.4%).[8] Other data show that youth are less likely than adults to adhere to PMTCT tenets.[5,8-13] A Kenya study found 8% of adult vs. 33% of adolescent mothers were not using ART, and 2% of adults' infants vs. 14% of adolescents' infants were not being given ARTs by their parents for PMTCT.[10]

Stigma has a detrimental effect on outcomes among pregnant adolescents.[14] Common fears among pregnant unmarried ALHIV include being seen while attending PMTCT clinics and the gossip that would follow.[15] Uninfected adolescents have also reported feeling stigmatized by their pregnancies, feelings of social isolation and loneliness, fear of family reaction, and experiences with derision and shaming meted out by ANC providers.[16-20] While HIV stigma is associated with a health condition, pregnancy stigma may be associated with perceived moral corruption via premarital sex.[21,22] Although the convergence of HIV and pregnancy-related stigmas may be understood implicitly, a lens of intersectionality has not been applied to address their potential combined effects on disclosure, social support, and PMTCT outcomes among pregnant ALHIV.[21,23]

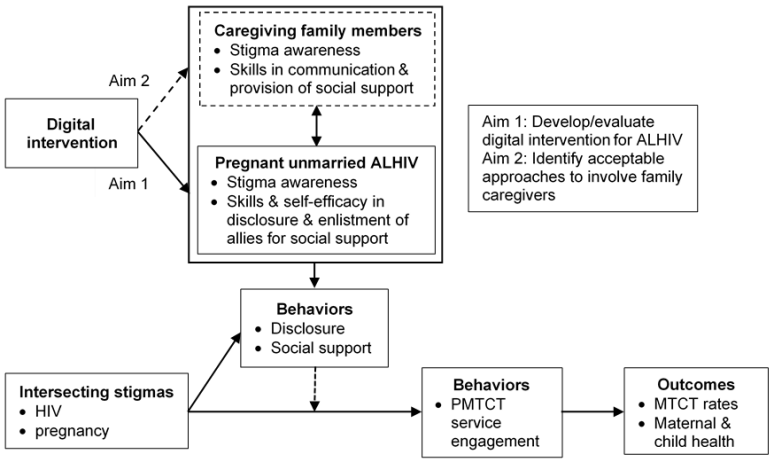
Disclosure and social support improve uptake of PMTCT services. Disclosure of HIV and pregnancy to family members increases social support and is important for PMTCT engagement.[24] [25-28] However, adolescents who receive their diagnoses alone may delay disclosure of their HIV status and/or pregnancy to family members, and thus do not receive needed support to engage in timely PMTCT care.[8,15,29] Family members (often a mother, grandmother, sister, or aunt) are a crucial source of support for pregnant adolescents.[16,29] Unmarried pregnant women are more likely to rely on support from family members than from a male partner.[30] Research is needed to identify effective strategies to promote and facilitate communication between pregnant ALHIV and their caregivers to improve their engagement in PMTCT care.

Few interventions exist to address stigma outcomes among pregnant ALHIV.[31,32] Only one study in South Africa has evaluated an intervention to address stigma among pregnant adult women living with HIV.[33] The intervention comprised of six group sessions (four antenatal, two postnatal) led by lay health workers. Two sessions focused on stigma by addressing communication with partners, HIV status disclosure, and ART adherence. While the intervention reduced HIV stigma,[33] it did not reduce MTCT or increase ART adherence or ART/PMTCT knowledge.[34] The limited impacts were attributed to the intervention's focus on individual factors rather than a multilevel approach that involved partners.[22,34]

Use of mobile health (mHealth) tools improves PMTCT uptake. Among pregnant adult women, SMS and phone calls have been found to increase PMTCT outcomes.[35-37] SMS approaches have also shown promise in lowering pregnancy rates among adolescents.[38] Studies show that SMS works well for reminders, [39-41] but if used alone they are limited in their ability to facilitate behavior change via support mechanisms or skills development.[42] Thus, in addition to SMS, other mHealth tools are needed to achieve desired outcomes.

There are no digital interventions to address PMTCT outcomes among pregnant ALHIV. Digital interventions include ehealth approaches, which use information and communication technologies for health-related purposes, and mhealth approaches, which use mobile devices for health-related purposes. They include interventions delivered via SMS, the web, social media, and smartphone apps. More recent approaches include gaming principles, interactive elements, simulations, and virtual reality. No studies have tested the impact of digital interventions on PMTCT behaviors/outcomes or HIV stigma among pregnant ALHIV. However, a growing number of studies highlight the promise of such interventions in supporting HIV-status disclosure,[43] engagement in care, and adherence to ART.[44-46] Most studies have been conducted in the U.S. among young men who have sex with men (MSM),[43-45,47,48] with only one conducted in Kenya that showed preliminary efficacy in reducing HIV risk and improving communication with parents among adolescents aged 11-14.[49,50] While youth access to mobile and smart phones continues to grow in many African countries, including Kenya,[51-53] breach of privacy via phone sharing is a key concern that threatens the viability of SMS and app interventions.[54] Still, recent studies indicate that adolescents are amenable to mHealth approaches to improve health. [55,56] Digital interventions with web-based components for knowledge and skills development, and SMS for reminders (coded for privacy), may offer an alternative, more ethically sound approach to facilitate behavior change.[39-41]

Figure 1. Integrated Conceptual Framework



Conceptual Framework. Intervention development is informed by an integrated framework, with adaptations from The Health Stigma and Discrimination Framework;[22] Turan's framework for the effects of stigma on maternal and child health;[14] the social ecological model (SEM);[57,58] Heaney and Israel's social networks and social support model,[59] and Bandura's Social Cognitive Theory (SCT).[60] In this study, we posit that intersecting HIV and pregnancy stigmas increase non-disclosure and inhibit social support, which, in turn, intensifies the negative direct effect of these stigmas on use of services to prevent MTCT and improve health outcomes. We propose to develop an intervention that will (1) raise awareness about these intersecting stigmas; (2) increase self-efficacy and communication skills for disclosure and enlistment of family caregivers as social support allies; and (3) counteract the effect of stigma on disclosure and social support among pregnant ALHIV. Ultimately, these improvements are expected to enhance PMTCT engagement and outcomes. Previous studies have shown that social support buffers the negative effects of stigma[61,62] and improving self-efficacy improves health among youth.[60]

Team's Prior Experience. The PI, **Dr. Luseno**, was the PI of a recently completed R01 that examined ethical issues in the conduct of adolescent HIV research in sub-Saharan Africa (R01MH102125) and a supplement to the R01 examining ethical issues in the implementation of medical male circumcision for HIV prevention among adolescents in Kenya (R01MH102125-S1). Dr. Luseno was also the PI on a previous R21 study to examine adolescent HIV prevalence, use of HIV health-related services, and barriers and facilitators to accessing care in Kenya (R21MH099923). The R01, supplement, and R21 were

all conducted in the Nyanza region. Co-Investigators (Co-Is) include **Dr. Gilbertson**, who led the qualitative component of Dr. Luseno's supplement. He also co-led a study in the U.S. to examine experiences among patients diagnosed during acute HIV infection and the ethical issues to consider when involving this population in clinical research (R21AI120549). **Dr. Kwaro** is based at KEMRI and was a Co-I on the ethics parent R01 and supplement. He has extensive knowledge about the local Kenyan health system and has led several HIV prevention/control, care, and treatment programs as a clinician and program manager. Currently, he leads a Gates Foundation funded ANC surveillance project in one sub-county within Siaya County. There are 1,263 pregnant adolescents aged 15-19 in this project. Of these, 63 (5%) are HIV-infected; half (32/63) are single. **Dr. DeRosier** is Chief Executive Officer at 3C Institute. She has extensive experience with development and implementation of both universal and targeted positive behavioral interventions for adolescents. Her recent research focused on developing and implementing evidence-based interventions via emergent technology and intelligent tutoring systems. She has served as PI and co-PI on several NIH-funded projects to develop culturally specific digital interventions. See Appendices B1-B3 for additional information about Drs. Luseno, Gilbertson, and DeRosier, including publications.

6. PROBLEM STATEMENT:
Nyanza has high rates of pregnancy among ALHIV and MTCT and youth are less likely to receive PMTCT services than adults. HIV- and pregnancy-related stigmas, non-disclosure, and lack of social support are key barriers to PMTCT engagement. In this study, we will develop and conduct a preliminary evaluation of a digital intervention to address the effects of the intersecting HIV and pregnancy stigmas on self-disclosure and social support among unmarried adolescents. We will also identify acceptable approaches to involve family caregivers. Our goal is to improve PMTCT outcomes among ALHIV.

7. JUSTIFICATION FOR THE STUDY:
First, we will develop a novel theory-informed digital intervention to mitigate the effects of two intersecting stigmas (HIV and pregnancy) on PMTCT behaviors among pregnant ALHIV, a vulnerable yet understudied population. Our intervention will include SMS, which has been found to work well for reminders,[51-53] and web-based elements to engage users and enhance the degree and depth of their interaction with the intervention content to increase learning and skills-building. Second, we propose a rigorous phased approach with end-user involvement to develop and evaluate the intervention. Third, we will explore with family caregivers of pregnant ALHIV acceptable approaches to involve them in providing support and to strengthen their communication skills. Although family caregivers are an important source of support for these young women, there is a dearth of research on strategies to help them build skills to effectively communicate with and provide needed support to their loved ones during this tumultuous time in the family unit. Fourth, we include bidirectional capacity building across our study team to strengthen skills in stigma research, qualitative analysis and manuscript development among Kenyan team members (KEMRI) and cultural competence and understanding with respect to digital intervention development among US team members (PIRE and 3C Institute).

8. STATE THE NULL HYPOTHESIS:
Not applicable. Consistent with the National Institutes of Health (NIH) R21 funding mechanism, our study is exploratory and developmental. Thus, no formal hypothesis testing will be conducted.

9. (a) **GENERAL OBJECTIVES**:

The main goal of our study is to collect data to understand the lived experiences of pregnant unmarried ALHIV, how to strengthen the supportive role of their family caregivers, and to use these data to develop a digital intervention to improve health outcomes for this vulnerable population.

(b) **SPECIFIC OBJECTIVES:**
Aim 1: To develop and evaluate a digital intervention for pregnant unmarried ALHIV aged 15-19 to increase awareness of stigma and its consequences; improve disclosure self-efficacy and skills; and facilitate enlistment of family caregivers as social support allies to enhance uptake of PMTCT services.

Aim 2: To identify acceptable approaches to increase awareness about stigma and enhance skills in communication and provision of social support among family caregivers.

10. METHODOLOGY:
(a) **Study site** (Geographical): The study will be conducted in Nyanza's Siaya and Kisumu Counties. Siaya is rural with a population of roughly 841,746.[63] Kisumu County is urban, consists of Kisumu City, and has a population of about 968,451.[64] Including urban and rural participants will ensure our approach is robust and unbiased, and broaden the applicability and relevance of our intervention.

(b) **Study design**: Our two-year study will consist of qualitative approaches for intervention development, and a mixed methods pilot study to assess the newly developed intervention's acceptability, usability, and preliminary efficacy (Aim 1). We will also conduct focus group discussions (FGDs) with family caregivers to identify acceptable approaches to strengthen their supportive roles (Aim 2). This formative work, done in partnership with the end users, is critical for the development of a feasible and effective digital intervention.

(c) **Study populations**
The **study components and populations** are as follows:
1. Individual interviews with pregnant ALHIV participants and joint interviews with pregnant ALHIV/caregiver dyads to inform initial digital intervention planning and development (Aim 1).
2. Focus groups with pregnant ALHIV participants to obtain feedback on sample digital intervention materials (Aim 1).
3. Pilot study with pregnant ALHIV participants who will test and evaluate the prototype (Aim 1).
4. Focus groups with ALHIV caregivers to identify ways to involve them (Aim 2).

Each type of participant group will be half from a rural area and half from an urban area. All participants will participate in only one research component.

Aim 1 adolescent participants: N=24 adolescents will participate in an IDI and N=24 adolescents will participate in a dyadic interview with a family caregiver **(Component 1),** N=32 adolescents will participate in an FGD (4 FGDs comprised of 8 participants each, **Component 2**), and N=30 adolescents will participate in the pilot study **(Component 3).** Inclusion criteria: All adolescent participants will be female, currently pregnant, unmarried, 15-19 years old and have been diagnosed with HIV and aware of this diagnosis. They will collectively have a range of disclosure experiences (disclosed pregnancy and HIV status to a caregiving family member, disclosed one of the two conditions, has not disclosed either condition). Exclusion criteria: An adolescent will be excluded if she: (1) does not meet all inclusion criteria, (2) already participated in a study activity, or (3) does not show understanding of consent based on our consent assessment.

Aim 1 caregiving family member participants (N = 24, Component 1): They will be the family member who participates in the dyadic interview with an ALHIV. Inclusion criteria: Caregiving family member (e.g., parent, guardian, grandparent, sibling or other relative) of a pregnant unmarried ALHIV who is aged 15-19. They will be age 20 or older and may be female or male. Exclusion criteria: Caregivers will be excluded if they: (1) do not meet all inclusion criteria, (2) already participated in a study activity, or (3) are a romantic/sexual partner or a family member of a romantic/sexual partner of a pregnant ALHIV (rather than a member of her family).

Aim 2 caregiving family member participants (N = 64, Component 4): Inclusion criteria: Like the Aim 1 caregivers, they will be a caregiving family member of a pregnant unmarried ALHIV who is aged 15-19, aged 20 or older, and may be female or male. They may or may not be the family member of an Aim 1 participant. They will participate in one FGD session. Exclusion criteria: Caregivers will be excluded if they: (1) do not meet all inclusion criteria, (2) already participated in a study activity, or (3) are a romantic/sexual partner or a family member of a romantic/sexual partner of a pregnant ALHIV (rather than a member of her family).

(d) Sampling

Sample size determination: Sample sizes for our qualitative research activities (IDIs, DIs, and FGDs) are consistent with guidance to reach saturation and previous experience.[65,66] Our study is not powered to detect statistically significant intervention effects on our behavioral outcomes. Rather, our focus is to assess the intervention's acceptability, usability, and whether it produces clinically meaningful improvements on our primary outcomes. Positive findings, even if not statistically significant, will provide preliminary evidence in support of conducting a larger pilot trial of this novel intervention. Nonetheless, based on enrolling 30 subjects, 80% power, and 10% two-sided type I error rate (Bonferroni corrected), the minimum detectable effect size in a pre-post comparison (paired t-test) of each subject's scores on our primary outcomes of 1) anticipated HIV stigma from family members, 2) internalized pregnancy stigma, 3) HIV disclosure self-efficacy, and 4) pregnancy disclosure self-efficacy is a Cohen's dz (standardized difference scores) of .59. This is considered a "medium" effect size. As a secondary outcome, we will assess safe disclosure behaviors to determine whether we can obtain valid and reliable measures of the incidence and timing of disclosure since this would be a primary outcome in a scaled-up trial of the intervention. Our proposed sample size and single pre-post intervention group design is appropriate for this pilot study's purpose of assessing time-related patterns and consistent with guidelines for assessing clinically meaningful improvements in outcomes.

Sampling procedure: We will use purposive sampling techniques to select ALHIV and caregivers from our urban and rural study settings based on inclusion criteria. Recruitment of pregnant ALHIV **(Components 1, 2, and 3):** For individual in-depth interviews (IDIs) and focus group discussions (FGDs), we will select adolescents who have disclosed and not disclosed their pregnancy and/or HIV status to a caregiver. For dyadic interviews (DIs), we will purposively select adolescents who have disclosed both conditions to their caregiver. Pilot study participants will not have disclosed at least one of the two conditions to a caregiver. In both our urban and rural sites, we will recruit participants from maternal and child health (MCH) clinics in public health facilities. Kisumu and Siaya County Directors of Health will assist us to identify public health facilities serving large numbers of pregnant ALHIV. As in our previous research, we will visit the facilities to seek assistance from MCH providers in referring potential participants to our study staff. To protect their privacy, MCH staff will inform potential participants (i.e., pregnant unmarried ALHIV aged 15-19) about our study and ask if they are interested in participating.

MCH providers will give interested individuals the following options: (1) give verbal consent to the MCH provider to allow their contact information to be shared securely with study staff, (2) be given contact information of the study staff so that the adolescent can call at her convenience, and/or (3) give verbal consent for the MCH provider to call study staff in their presence to schedule a meeting. Providers assisting with recruitment will be trained in human subjects protections and given a script to use when informing potential participants about the study. We will adjust our recruitment procedures based on any new clinic/hospital protocols that have been implemented to mitigate the spread of COVID-19. Providers will receive financial support to assist with recruitment (e.g., for cell phone airtime and transport).

We will also use snowball sampling techniques to recruit participants. We will ask ALHIV and caregivers who participate in study activities if they are willing to assist with recruitment. To ensure the privacy of potential participants, we will provide participants who are willing to assist with recruitment with up to two flyers each to pass on to potentially eligible ALHIV and caregivers in their communities. The flyer will include instructions for individuals who are interested in participating in the study. We may also advertise the study to pregnant ALHIV by placing posters with a brief study description and contact information in health facilities and other public venues that interested pregnant ALHIV may use to contact research staff. We used this procedure in our previous study.

Our staff will be trained on COVID-19 protective measures (i.e., wearing masks, washing hands, and keeping a safe distance) and on how to explain these measures to potential participants using culturally appropriate terms. They will be provided with surgical masks and hand sanitizer for themselves and to offer to participants they interact with. Staff will meet participants at a location that is comfortable, convenient, and private for the potential participants. The staff will use a script to provide potential participants with information about the study, answer questions, and use a screening questionnaire to confirm eligibility for the research activity. They will enroll eligible participants while meeting our purposive sampling goals of (1) having equal numbers of participants from the rural (Siaya) and urban (Kisumu) counties, and (2) having the HIV and pregnancy disclosure experience appropriate to the research activity. For the DIs, we will not recruit ALHIV who decline to identify a caregiver to invite for the DI. Participants will participate in one study activity. Regular meetings during the recruitment period will be held by research staff and clinicians assisting with recruitment to identify and overcome difficulties during this phase. These strategies worked well for the team in a previous study.[15,66]

Recruitment of caregivers **(Components 1 and 4):** Caregiving family members will be a parent, guardian, grandparent, sibling, or other relative of a pregnant ALHIV who is responsible for the adolescent's care, food, and/or shelter. Study staff will ask adolescents who have disclosed their HIV status and pregnancy to family member(s) if there is a caregiver whom they recommend being invited to participate in the dyadic interview or focus groups. ALHIV will be informed that recommending a caregiver for a dyadic interview or focus group is optional and not required for study participation. ALHIV will give their permission for their caregivers to be recruited for the study (either for a dyadic interview or for the Aim 2 FGD). We expect that some pregnant ALHIV who have disclosed both conditions will decline to nominate a caregiver and for their safety we will not ask those who have not disclosed either or both conditions to nominate a caregiver. Only ALHIV who have disclosed their conditions and the caregiver to whom they have disclosed their conditions will be invited to participate in dyadic interviews.

As needed, in order to achieve our Aim 2 sample targets **(Component 4),** we will recruit additional family member caregivers of pregnant unmarried ALHIV aged 15-19 from the community and clinics. For

example, we will seek assistance from providers to recruit eligible caregivers in their catchment areas. We also will place posters with a brief study description and contact information for study staff in the health facilities and other public venues that interested caregivers of pregnant ALHIV may use to contact research staff. We will recruit only caregivers who already are aware they are caring for an adolescent who is both pregnant and living with HIV. We will conduct eight FGDs in Aim 2 (4 rural, 4 urban; 8 participants per FGD; n=64) in two rounds. In round 1, we will present Aim 1 findings, obtain caregivers' perceptions about whether the findings resonate with their experiences, and explore acceptable approaches to strengthen caregivers' skills. In round 2, we will present the final Aim 1 prototype and obtain caregivers' views, including about the acceptability of a complementary digital intervention for caregivers.

Retention of participants: Adolescents and caregivers who participate in individual in-depth interviews (IDIs), dyadic interviews (Dis), and focus groups (FGs) will participate in one research activity; thus, we will not have a retention plan for them. Adolescents who participate in the pilot study will take a follow-up survey two weeks after exposure to the intervention. The short time interval of two weeks will help to ensure participants are not lost to follow-up. In addition, to help us retain these participants, we will obtain participant locator information, including contact information, and set up the two-week appointment in advance. One week before their appointment, study staff will send an SMS to remind participants about their upcoming appointment. A day before their appointment, staff will place a phone call to participants to arrange a time and place to meet for the follow-up appointment. All participants, including caregivers, will be given an incentive of USD $10 for each session.

(e) Procedures

Overview of Procedures

Summary of data collection: Aim 1 will consist of three phases. In Aim 1 Phase 1, we will conduct individual in-depth interviews (IDIs) with pregnant ALHIV and dyadic interviews (DI) with pairs of pregnant ALHIV and their family member caregiver. In Aim 1 Phase 2 we will conduct focus group discussions (FGDs) with pregnant ALHIV. In Aim 1 Phase 3 we will carry out a pilot study with pregnant ALHIV serving as prototype testers and will collect survey data (baseline and two-weeks post-intervention) and qualitative data (participant thoughts and field staff notes). In Aim 2, we will conduct two rounds of FGDs with family member caregivers of an ALHIV.

What Participants Will Do

Individual in-depth interviews (IDIs) of adolescents (Aim 1 Phase 1, **Component 1**): All IDIs will be conducted by trained, experienced interviewers able to speak fluently in the local languages (Luo, Swahili, and English). The research team will develop a semi-structured interview guide. Questions asked of the pregnant ALHIV will include ones pertaining to their experiences disclosing their HIV and/or pregnancy status to caregiving family members, receiving support from caregivers, with stigma due to their HIV and/or pregnancy status, and perspectives about SMS and digital intervention features, images, and preferences. IDIs will be conducted at venues that offer privacy and are quiet, convenient, and comfortable for participants. Each interview will take about 60-90 minutes.

Dyadic Interviews with adolescents and caregivers (Aim 1 Phase 1, **Component 1**): Research staff will use the same procedures for conducting the DIs as described above for the IDIs (i.e., semi-structured interview guide, private and convenient venues for the interviews, 90-minute sessions). However, in these interviews, the adolescent and their caregiver will be interviewed together. Research staff will ask

them about their disclosure experiences, what could have improved the experience, the best ways to involve caregivers, and advice they have for people in a similar circumstance.

The research team will use the IDI and DI findings, led by our 3C Institute collaborators, to develop initial specifications and mock-ups of the digital intervention.

FGDs with adolescents (Aim 1 Phase 2**, Component 2**) and caregivers (Aim 2, **Component 4**): For Aim 1 there will be 4 FGDs (8 participants each) conducted with pregnant ALHIV (2 rural and 2 urban). For Aim 2, there will be 4 FGDs (8 participants each) conducted with caregiving family members (2 rural and 2 urban) in Round 1 and 4 FGDs in Round 2 (2 rural, 2 urban). FGD sessions will be facilitated by a trained KEMRI moderator fluent in the local languages who will use a semi-structured guide. Each session will last up to two hours. The adolescents will be asked for feedback on the content and flow of the intervention module and their opinion on the mock-ups (e.g., appropriateness, realism, appeal, and plans for using text messaging). Caregivers in Round 1 will be asked about our plans for developing a digital intervention for ALHIV and approaches for involving family caregivers. Caregivers in Round 2 will be asked for feedback about the final Aim 1 intervention prototype and views on a potential complementary digital intervention for caregivers. All FGDs will be conducted in a location providing privacy and confidentiality.

Using Aim 1 findings, the research team will develop an intervention prototype. As part of this process, PIRE and KEMRI staff will test versions in order to finalize the prototype.

Pilot study with adolescents (Aim 1, **Component 3**): The pregnant ALHIV participants will complete a 40-50-minutes baseline survey that includes questions about demographics, HIV and pregnancy stigmas, and disclosure. All participants will receive a one-on-one intervention session in which they will be provided with a study mobile phone with internet access, guided on how to access the prototype intervention, and instructed to go through the intervention. Research staff will take notes of observations made while participants are using the app. Immediately after participating in the intervention, the adolescents will complete a questionnaire asking about the intervention's acceptability and usability. Intervention sessions may last up to two hours. Altogether, the baseline data collection and intervention session will last approximately 3 hours. Participants will take a follow-up survey two weeks after the intervention session, which will last about 40-50 minutes.

All participants (Aims 1 and 2, **Components 1 through 4**): The study will collect private identifiable information from all participants. Socio-demographic data (e.g., age, gender, educational attainment) and written consent forms (containing participant names) will be collected from all participants. Participants in the interviews and pilot study will be asked questions about their own lives and experiences.

COVID-19 Prevention Protocols (all participants): Dr. Kwaro (KEMRI co-investigator) is overseeing operations of a research project monitoring HIV infections among pregnant women in Siaya County. We will follow his study's protocols (adapted as needed), which are compliant with Kenya's Ministry of Health guidelines for COVID-19 prevention. Study staff and research participants will be screened for COVID-19 symptoms before engaging in study procedures (taking temperature, screening for symptoms, and compulsory handwashing/sanitizing). Staff or participants who screen positive will be directed to appropriate testing and health care resources. Study staff will receive training on COVID-19 mitigation measures. Staff and participants will be required to wear face masks during all face-to-face interactions,

follow hand hygiene protocols, and adhere to physical distancing rules. Staff will sanitize data collection tools. Data collection activities will be conducted in open outdoor spaces whenever feasible and when privacy can be ensured. When that is not possible, the activities will be conducted indoors with adequate ventilation.

11. DATA MANAGEMENT:

Data Collection and Management: Data sources will include electronic data files, audio-recordings, transcripts, and field notes obtained from research activities which will include interviews, focus groups, and surveys. Research team members will audio-record the interviews and focus groups and take notes. All audio recordings will be transcribed and translated. The research team will develop and use codebooks for each qualitative research activity to analyze the data. For the pilot study, the research team will analyze the pre- and post-treatment questionnaire data to assess if the intervention produced clinically meaningful improvements on outcomes of interest. Participants will complete a survey at baseline, immediate post-intervention, and two-week follow-up. We will use an adaptation of the user version Mobile Application Rating Scale (uMARS),[79] modified for our study, to assess the intervention's acceptability [44,46] and usability.[44,67] Other measures, based on our conceptual framework (**Fig. 1**), will include demographics, stigma (HIV: anticipated from family members,[68] internalized,[69,70] coping;[71] pregnancy: internalized[72]), disclosure self-efficacy,[73] and disclosure to family members.[74] Survey data will be collected using computer-assisted interviewing (CAI) techniques on secure password-protected devices. All study data will be transferred from data collection devices to KEMRI's secure servers daily. Data will be transferred from KEMRI to PIRE as encrypted data files. At PIRE, the data will be stored on secure servers. Only research staff authorized by the PI (Dr. Luseno) and Co-PI (Dr. Kwaro) will have access to the data. PIRE staff will conduct further data cleaning, coding, and data analysis.

12. ETHICAL CONSIDERATIONS

(a) **Human Subjects**

Informed Consent: All study participation will be voluntary. Informed consent will be obtained from participants by trained research staff at each stage of the recruitment and enrollment process. Information provided as part of the consent process will include the purpose of the research, study procedures, explanation of possible risks and safeguards, and explanation that participation is voluntary.

Potential participants who are identified by MCH providers will be offered options about how to connect the individual with study staff (giving verbal consent for providers to share the person's contact information with study staff, receiving contact information of study staff, or allowing the provider to call study staff to schedule a meeting). Research staff will contact potential participants to introduce themselves and provide information. Individuals who are still interested in participating will be invited to meet in private where screening and consent procedures will be administered. Following a script, research staff will obtain verbal consent from individuals prior to screening them for study eligibility. Study staff then will obtain written informed consent from each eligible individual before the person participates in any research activity. Staff will administer an assessment of adequate understanding of the consent information, which we have done in previous research. For additional protection of participants in this study, all research staff will receive training on protection of human subjects including on confidentiality, the ethical conduct of informed consent procedures, administering the assessment of consent comprehension, and reviewing assessment answers and consent form information with the adolescent. Moreover, research staff will be experienced in conducting HIV-related studies with vulnerable youth, and skilled in counseling vulnerable youth, identifying distressed youth,

and interacting with the caregivers of vulnerable youth. They will also be knowledgeable about the study sites, cultural nuances, and fluent in local languages.

Request for waiver of parental consent and justification: We are requesting a waiver of parental consent to protect the confidentiality of adolescent participants, including those who are 15-17 years old, who will not have disclosed their HIV and/or pregnancy to their parents. Involving parents of those who have not disclosed their HIV and/or pregnancy status in the consenting process would result in a breach of confidentiality. Pregnant unmarried ALHIV is an understudied, underserved, and hard-to-reach population. Studies are urgently needed to better understand their lived experiences, the barriers they face in, and factors that facilitate, disclosure and uptake of services. The goal of our study is to examine these issues and to develop an approach to enhance disclosure to caregivers and thereby uptake of critical health services. Our study procedures balance the need to inform caregivers about the study without breaching the confidentiality of adolescent study participants.

We are requesting IRB approval to allow youths 15-17 years old to give consent for themselves and to not obtain parent/guardian consent for those youths. In Kenya minor adolescents are considered emancipated minors if they are pregnant, heading a household or are parents and are thus treated as adults [See National AIDS and STI Control Programme (NASCOP) and Kenya Medical Research Institute (KEMRI) (2015). Guidelines for Conducting Adolescents Sexual and Reproductive Health Research in Kenya. http://icop.or.ke/wp-content/uploads/2016/10/Adolescents-Guidance-on-HIV-SRH-Research.pdf.] However, as a culturally appropriate courtesy to the families in Kenya, and only with permission from the adolescent participant, we will inform parents, guardians, and/or household heads about the study and the 15-17-year-old adolescent's participation. While doing so, research staff will describe the study in a very general way that will not reveal undisclosed information about the adolescent. Research staff will be trained to ask all participants if they would like the staff to provide this information to their parent. The staff will be available to answer any questions from the adolescents and parents, and they will be trained to give the adolescent and parent time to consult with each other alone if the adolescent seems to want that. In addition, as stated in the consent form, at any time, a participant may change their mind and withdraw from the study. We have successfully used similar procedures in previous studies.[15,75]

Request for waiver of documentation of informed consent: We plan to obtain verbal consent without written documentation for participants to be asked screening questions to determine their eligibility to participate in the study. The reason is that the only record linking the subject and the research would be the consent document the main risk for that person would be a risk of confidentiality.

Risk of inadvertent disclosure of HIV and/or pregnancy status: The young woman's HIV status or pregnancy could be inadvertently revealed to family or community members and result in her experiencing stigma. This could happen if someone who does not already know about the adolescent's pregnancy and/or HIV status were to learn that the adolescent or a caregiver is participating in a study for pregnant ALHIV and their caregivers. Accidental disclosure also could occur if a bystander were to overhear an interview or other data collection session in which HIV and/or pregnancy status is revealed. Although participants in the FGDs and pilot study interviews will not be asked personal questions, it is possible that some participants could reveal their HIV and pregnancy status when answering questions. A potential consequence of inadvertent HIV or pregnancy disclosure is violence from a partner, family member, or other person who is upset or who blames the young woman. In addition, adolescent or

caregiver participants could worry about such accidental disclosure occurring, which could result in them experiencing stress and anxiety.

Risk of emotional distress during data collection sessions: Some of the adolescent and caregiver participants in the interviews or pilot study could feel uncomfortable or emotionally distressed answering questions about themselves or their family member being pregnant; being HIV-infected; or experiencing problems regarding stigma, disclosure or social support. It also is possible that some participants may think about and disclose upsetting events (e.g., sexual abuse, intimate partner violence, or interpersonal conflict) during the data collection session. FGD participants will not be asked personal questions, but some individuals could potentially think about personal and sensitive thoughts during the research activity.

Safeguards for inadvertent disclosure of HIV or pregnancy status: Interview, FGD, and pilot study sessions will be conducted at venues that offer privacy and confidentiality. IDIs and pilot study sessions will be conducted individually. Research staff will be sensitive to participants having various disclosure circumstances and to the potential risks of accidental disclosure. We will use our experience from previous studies[15,66,75-78] when entering homes and communicating with household members to ensure our participants' safety and confidentiality. Only caregivers who know both conditions (HIV-positive status and pregnancy status) of the adolescent they are caring for will be recruited to participate in the dyadic interviews. We will follow procedures to protect data security (described below). We have not come across in any of our previous studies[15,66,75-78] situations in which an adolescent became exposed to violence due to participating in our study. However, we will employ research field staff who are either trained as nurses or counselors or experienced in data collection; will be from the local region and knowledgeable about cultural nuances; and will have experience with HIV studies and working in rural and low-income settings. Like prior studies, staff will receive further training for this study, will have a list of resources to help participants in need, and will be prepared to address potential adverse situations.

Safeguards for emotional distress during data collection sessions: Participants may choose to not answer particular questions and to stop their study participation at any time. Field staff will be trained to offer referrals, based on available services within the community, if a young woman were to disclose she has been a victim of sexual abuse, violence or other traumatic experience. Staff will be trained to discuss sensitively the young woman's disclosed experience. Field staff also will be trained to monitor for emotional upset or anxiety during or as a result of the data collection session among any of the participants and to offer support and referrals for services, if they are available. In collaboration with our KEMRI partners, we developed a list of available resources and services for referral purposes in our previous study for adolescent participants in need of psychological, social and medical services. We will update the list and require research staff to distribute a copy to **all** study participants at the conclusion of data collection activities. For adolescents who are identified as distressed, express a need for services, or have not disclosed their pregnancy and/or HIV status to a caregiver, research staff will provide active referrals to services in the community, e.g., antenatal care (ANC), prevention of mother-to-child HIV transmission (PMTCT), HIV treatment and care, counseling, and support with facilitated disclosure.

Data security: Unique ID codes will be attached to data (including transcripts and audio-recording files) instead of participant names or other personal identifiers. Data, any lists of names and ID codes, and consent forms will be stored in locked cabinets (if paper) or password-protected (if electronic). No

reports will link individuals' names with data; study results will be reported as aggregate data. Research staff will have access to data only on a need-to-know basis.

Study monitoring and oversight: The PI will obtain approval for the study from the PIRE and KEMRI IRBs. Research staff will receive training in protection of human subjects, research protocols, use of the study's Data Safety and Monitoring Plan (DSMP), and maintaining participant confidentiality. Input will be obtained from the Kenyan team to ensure our plans for monitoring participant safety are appropriate to the local situation, and staff will be trained on the procedures. The PI, co-investigators, and study staff are experienced in conducting research in sub-Saharan Africa, including in the Nyanza region in Kenya and in data collection with HIV-infected adolescents, pregnant adolescents, and family member caregivers. The PI is experienced in monitoring participant safety of HIV-infected, pregnant, and emotionally distressed youth and overseeing field work in Kenya. The study will receive review and oversight from the IRBs. Details of our DSMP are provided in an attachment.

Benefits: Participants may experience personal satisfaction from communicating with researchers about topics relevant to pregnant ALHIV such as stigma, disclosure and family support; being treated as knowledgeable stakeholders; and being part of a study that could potentially help people in similar circumstances of need. The adolescents who participate in the pilot study may benefit from receiving the digital intervention session which will be designed to help adolescents like them improve stigma knowledge and coping skills, HIV and pregnancy disclosure skills, and enlisting support of caregiving family members. The study's risks are reasonable in relation to the potential benefits to participants and others.

(b**) Animal Subjects.** Not applicable.

13. DATA ANALYSIS PLAN

Qualitative Data. Audio recordings of the sessions will be transcribed and translated. Field notes will include detailed notes taken by research staff during sessions. All interview transcripts will be deidentified and assigned ID numbers. Transcripts will be read by research staff. Using MAXQDA, deductive codes will be applied to segment narratives into a priori conceptual categories (e.g., text describing how disclosure occurred). Next, we will apply inductive codes for each conceptual category (e.g., reasons ALHIV delay disclosure of pregnancy to caregivers). We will meet virtually bimonthly to discuss coding, emerging and overarching themes, and to organize the data into thematic groups. We will examine code frequencies across transcripts to identify the most salient themes and create text matrices to highlight the co-occurrence of deductive and inductive codes. We will write summary reports to describe themes, including illustrative narratives that will be the basis for the intervention mock-ups. Analysis will be ongoing to determine whether we are collecting the data we need, if changes to interview guides are needed, and data saturation.

Quantitave Data: We will use SAS to summarize the quantitative data. Frequencies and measures of central tendency will be calculated for demographics, usability, and acceptability. We will conduct descriptive analysis on data collected at two time points to assess time-related patterns and clinically meaningful improvements in measures. Our study is not powered to detect statistically significant intervention effects. Our goal is to assess maintenance/persistence intervention effects after a short duration exposure.

14. EXPECTED APPLICATION OF THE RESULTS:

The research has a high social value and the potential to benefit adolescents and families in both rural and urban areas of a region with high prevalence of HIV and adolescent pregnancy. The study will develop a digital intervention that will be designed to address stigma affecting pregnant unmarried ALHIV, facilitate skills for disclosure and enlisting family caregiver support, and improve engagement in PMTCT services

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