Protocol

"*PrEP My Way*": A Novel PrEP Delivery System to Meet the Needs of Young African Women

Version 2.0

20 January 2021

Funding:
US National Institute of Mental Health
(R34MH122362)
NCT04408729

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ACRONYMS

ART	Antiretroviral therapy
CAB	Community advisory board
DBS	Dried blood spots
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act of 1996
HIV	Human Immunodeficiency Virus
MSM	Men who have sex with men
PEPFAR	President's Emergency Plan for AIDS Relief
PrEP	Pre-exposure prophylaxis
RA	Research assistant
RCT	Randomized controlled trial
RCTP	KEMRI Research Care and Training Program
SMS	Short message service
STI	Sexually transmitted infection
SUS	Systems usability scale
TFV-DP	Tenofovir diphosphate
UTAUT	Unified Theory of Acceptance and Use of Technology

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Abstract
Young women in sub-Saharan Africa are a vulnerable population in terms of HIV acquisition with ~7,000 new infections occurring per week. Oral daily pre-exposure prophylaxis (PrEP) is a highly effective means of HIV prevention when taken regularly. Early experience with the global rollout of PrEP in this population indicates enthusiasm for PrEP, but also barriers to adherence and program retention.

PrEP My Way is a novel PrEP delivery system consisting of clinic-based PrEP initiation, followed by peer-delivered kits for HIV self-testing, PrEP refills, vaginal swabs for gonorrhea and chlamydia self-sampling, pregnancy tests, and contraception refills, if desired. Based on Social Cognitive Theory, our overall hypothesis is that *PrEP My Way* will overcome critical stigma and structural barriers that currently limit PrEP use and thus empower young women to promote their sexual health.

Introduction/Background
We will first develop, tailor, and refine *PrEP My Way* for use with young women in Kisumu, Kenya (Aim 1). We will use a client-centered, iterative approach, involving individual interviews and focus group discussions to optimally design the *PrEP My Way* kit (with instructional materials) and peer delivery system (including communication and kit delivery plans). We will then test the intervention for feasibility, acceptability, and preliminary impact on PrEP adherence and program retention (Aim 2). We will randomize up to 150 Kenyan women to *PrEP My Way* versus standard of care (i.e., clinic-based delivery of PrEP and sexual health services) and follow them for 6 months. Feasibility will be assessed by receipt of the kit at 1, 3, and 6 months and ability to use its components per protocol. Acceptability will be determined through a mixed-methods interview at 6 months. Preliminary impact will be evaluated by dried blood spot tenofovir levels (adherence) and kit use/clinic attendance at 6 months (retention) as primary outcomes. Mediators and moderators of PrEP use (e.g., empowerment and mental health) will be explored through questionnaires at baseline and 6 months.

Design: Formative work, followed by a pilot randomized controlled trial (RCT) of *PrEP My Way* versus standard of care (1:1)

Population: Young (16-24 years old) sexually active women who are interested in taking PrEP and own a phone

Study site: Kisumu, Kenya

Specific aims:
1. Develop *PrEP My Way*. Using a client-centered approach, we will iteratively conduct individual interviews and focus group discussions with up to 70 Kenyan women (age 16-24) or other relevant community members to optimally design *PrEP My Way* (the kit with instructional materials) and peer delivery system (including phone communication and kit delivery plans).

2. Assess *PrEP My Way* for feasibility, acceptability, and preliminary impact on PrEP adherence and program retention. We will randomize up to 150 Kenyan women (age 16-24) to *PrEP My Way* versus standard of care (i.e., clinic-based delivery of PrEP and sexual health services) and follow them for 6 months. Feasibility will be assessed by receipt of the kit at 1, 3, and 6 months and ability to use its components per protocol. Acceptability will be determined through a mixed-methods interview. Preliminary impact will be evaluated by dried blood spot tenofovir levels (adherence) and kit use/clinic attendance at 6 months (retention). Potential

influencing and mediating socio-behavioral factors will be explored with questionnaires at 0 and 6 months.

Justification for the study

Young women are a highly vulnerable population in terms of HIV acquisition given 1) limited access to sexual health information and services in many settings [1], 2) limited ability to negotiate condoms in many sexual relationships [2], 3) high risk for HIV acquisition in the setting of gender-based violence which can be very common [3], and 4) the 2-8X increased efficiency of HIV transmission from men-to-women compared to women-to-men [4]. Young women currently account for three-quarters of all new HIV infections in sub-Saharan Africa— a figure that translates to ~7,000 new infections occur per week [5]. Moreover, with the impending youth bulge, the adolescent population will reach >300 million by 2050 [6]. Clearly HIV prevention tools are needed for this population, and PrEP (current recommended as daily oral 300mg tenofovir/200mg emtricitabine) is in many ways an ideal option. It is safe and effective, it can be taken discretely, and it does not require negotiation with sexual partners [7]. And, young women want effective HIV prevention options as evidenced by 86-95% uptake of PrEP in two recent demonstration projects in southern Africa and Kenya [8, 9], as well as numerous advocacy campaigns [10].

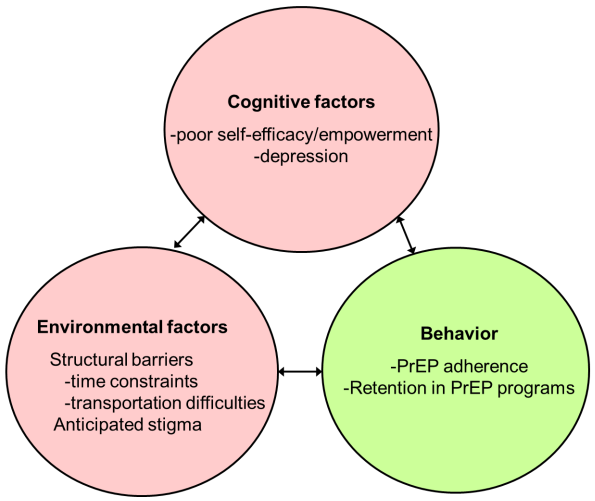
Despite the advantages of PrEP, adherence and retention in PrEP programs have been challenging for young women. In two phase III clinical trials of PrEP, plasma tenofovir was detected in only 28-36% of women 18-25 years old [11, 12]. More recently, protective plasma levels of tenofovir were only seen in 38% of young women participating in a demonstration project in South Africa [13]. Additionally, only 10% of young women were still picking up PrEP at 6 months in the above-noted Kenyan demonstration project, despite the high uptake [9]. Novel means to support ongoing use of PrEP and retention in care will be critical to successful HIV prevention efforts in this population.

Two significant and unaddressed barriers to PrEP among young women in sub-Saharan Africa relate to stigma and structural barriers to PrEP access. Numerous implementation projects (e.g., through the PEPFAR-supported DREAMS Initiative) and academic studies are ongoing to address the important, fundamental need for information about PrEP and demand creation [14]. However, two additional barriers are significant impediments to the PrEP rollout among young women and warrant intervention development. Specifically, perceived stigma (e.g., being judged as promiscuous by older healthcare workers or in the community) and structural barriers (e.g., getting to clinics during regular business hours, funds for transportation) remain major factors that prevent women from accessing and persisting with PrEP [15]. These factors account for the majority of PrEP non-use in an ongoing study conducted by the investigators of this protocol (Monitoring PrEP for Young Adult Women [MPYA]; NCT02915367).

Stigma and structural barriers have been a challenge among all populations worldwide, yet creative solutions have arisen. In the US, for example, access for men who have sex with men (MSM) has been improved through provider awareness and education [16], as well as a novel home PrEP delivery system [17]. The latter, called PrEP@Home includes tailored pictorial and video instructions for specimen self-collection, mail in kits for all recommended lab tests (i.e., HIV, syphilis, chlamydia, gonorrhea, creatinine), and a self-completed electronic survey to assess behavioral components of care, such as medication adherence and tolerance. PrEP@Home has been found to be acceptable and perceived as helpful for persistence with PrEP. Novel approaches are needed now for young women in sub-Saharan Africa.

PrEP uptake is also limited by the lack of concurrent provision of testing for other sexually transmitted infections (STIs) and contraception. Young women have many sexual health needs. Undergoing clinical exams to test for STIs and seeking contraception take time, which may be limited for many young women because of school, work, or family responsibilities. Moreover, young women may be hesitant to pursue these services because of fear of judgement (e.g., being seen as promiscuous). These barriers are in many ways the same as those for PrEP. And yet, women greatly desire STI testing and contraception. Indeed, they may be even more motivated to seek these services compared to PrEP [18, 19]. Several forms of "multi-purpose technologies" are under development to provide co-formulated PrEP and contraception [20]; however, co-provision of these services may serve a similar function and is possible with currently available products.

Figure 1. Social Cognitive Theory underlying the *PrEP My Way* intervention

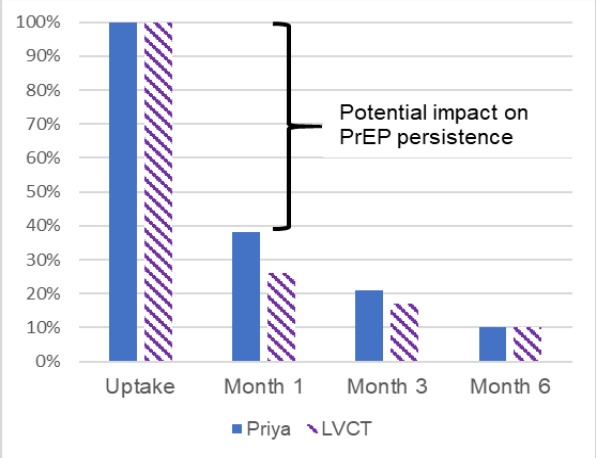


Social Cognitive Theory provides a useful framework for developing effective interventions to overcome the barriers young women face. Social Cognitive Theory posits that people acquire and maintain particular behavioral patterns through the interaction of three factors: environment, personal factors, and behavior [21-23]. Behavior is not simply the result of the environment and the person, just as the environment is not merely a function of the person and behavior. In a review of theories underlying HIV prevention interventions for young people in sub-Saharan Africa [24], Social Cognitive Theory was highlighted as favorable because it includes the influence of contextual and structural factors on an individual's behavior (unlike other commonly used theories, such as the Health Belief Model and Theory of Reasoned Action/Planned Behavior). As shown in Figure 1, *PrEP My Way* addresses the environmental factors (i.e., structural barriers and stigma) through personalized delivery of the kit at a time convenient for the young woman taking PrEP. Cognitive factors (i.e., self-empowerment and depression) are addressed through peer support and self-driven care; this approach has been effective in other peer-based, community delivery models to provide post-natal, HIV-related care in Uganda [25] and HIV testing among female sex workers in Uganda and Zambia [26, 27]. Ultimately, these factors interact with each other and the behavior of PrEP adherence and retention in PrEP programs.

Interventions are specifically needed for young women to persist with PrEP use and to reduce the burden of PrEP delivery in existing healthcare facilities. As shown in Figure 2, numerous recent demonstration projects and studies (e.g., PrIYA [28], LVCT Health [9]] have seen steep drop offs in PrEP use among young women after uptake. While many women make a very rational choice to discontinue PrEP (e.g., if they do not have an ongoing need for HIV prevention or they are adequately protected through some other prevention tool, like condoms), others want to continue with PrEP, but struggle due to factors such as stigma and structural barriers (see above). Much of this drop off could be attenuated through interventions aimed at PrEP persistence (i.e., adherence and program retention).

Moreover, the need and demand for PrEP among young women may well be overwhelming for traditional delivery structural. For example, PEPFAR estimated >250,000 young women need effective HIV prevention interventions to facilitate epidemic control [29]. Given the safety and ease with which PrEP can be prescribed, methods to simplify its delivery are desirable and promising, including the use of HIV self-test kits to spread out clinic visits (as is being explored by the investigators of this protocol in another study, NCT03593629). Importantly, the largest expense involved with PrEP provision is staffing [30]; thus, community-based PrEP delivery through lay health workers (i.e., peers) has the potential to be cost-effective. Thus, interventions that simultaneously ease the burden on healthcare infrastructure and overcome environmental and cognitive barriers to PrEP persistence are well poised to have high impact on PrEP use and ultimately HIV prevention.

Figure 2. Potential impact from an intervention aimed at PrEP persistence



Client-centered design increases the likelihood of the intervention uptake and use. Client-centered design is a framework of processes in which user characteristics, usability goals, environment, tasks, and workflow of a product, service, or process are given extensive attention at each stage of the design process [31]. Client-centered design can be described as a multi-stage problem-solving process that not only requires designers to analyze and envision the way users are likely to consume a product, but also to validate their assumptions with regard to the user behavior in real world tests. These tests are conducted with actual users at each stage of the process, ensuring that development proceeds with the client as the primary focus [32]. The overarching goal of this approach is to increase product usefulness and usability [33]. This protocol will therefore place the client at the center of the development process, thus promoting interest in PrEP and supporting persistence over time.

In sum, young women need and want PrEP, yet stigma and structural barriers are inadequately addressed barriers that are limiting their ability to persist in PrEP use with high adherence and program retention. *PrEP My Way* is a young woman-centered intervention that helps make PrEP more accessible, while also promoting ready use of other desired sexual health services—STI testing and contraception. The intervention is grounded in Social Cognitive Theory, addressing key environmental and cognitive factors influencing PrEP adherence and program retention. *PrEP My Way* is thus poised to have high impact on HIV prevention among young women in sub-Saharan Africa by reducing the large drop offs in PrEP use seen in current implementation programs.

General Objectives

Overall design. We will first develop, tailor, and refine *PrEP My Way* for use with young women in Kenya (Aim 1). We will then test the intervention for feasibility, acceptability, and preliminary impact on PrEP adherence and program retention in a pilot RCT (Aim 2).

Specific Objectives

1. Develop *PrEP My Way*. Using a client-centered approach, we will iteratively conduct individual interviews and focus group discussions with up to 70 Kenyan women (age 16-24) or other relevant community members to optimally design *PrEP My Way* (the kit with instructional materials) and peer delivery system (including phone communication and kit delivery plans).

2. Assess *PrEP My Way* for feasibility, acceptability, and preliminary impact on PrEP adherence and program retention. We will randomize up to 150 Kenyan women (age 16-24) to *PrEP My Way* versus standard of care (i.e., clinic-based delivery of PrEP and sexual health services) and follow them for 6 months. Feasibility will be assessed by receipt of the kit at 1, 3, and 6 months and ability to use its components per protocol. Acceptability will be determined through a mixed-methods interview. Preliminary impact will be evaluated by dried blood spot tenofovir levels (adherence) and kit use/clinic attendance at 6 months (retention). Potential influencing and mediating socio-behavioral factors will be explored with questionnaires at 0 and 6 months.

Design and Methodology

Study setting. Both aims of this protocol will take place in Kisumu, Western Kenya. This area is largely rural with an urban center and a total population of ~1,000,000. HIV prevalence is 21% among women. This study will be run under the KEMRI Research Care and Training Program (RCTP, a comprehensive HIV prevention, care and treatment program working in 100 clinics in Western Kenya). The RCTP is staffed by clinicians, pharmacists, counselors, community outreach officers, and laboratory technicians who are trained to provide routine health services, including HIV testing, PrEP, STI testing and treatment, and contraception. It has supported several projects focused on young women, as well as family planning/HIV integration studies (e.g., MPYA, PrIYA).

The primary recruitment site for both aims will be Lumumba Sub-County Hospital ("Lumumba Clinic"), which is located next door to the RCTP. PrEP is included in the Kenyan National HIV Prevention Revolution Road Map [34], in which young women are identified as a priority population, and available at no charge through Lumumba Clinic and other public facilities. A total of 438 young women have received PrEP at this facility, making recruitment highly feasible. Contraception and STI testing/treatment (typically in the setting of symptoms, not routine screening) are also available free of charge. Recruitment may also occur through Kisumu County Hospital, which has a similar clinic and is located a 5 minutes-drive from our study offices.

Aim 1. Develop the *PrEP My Way* intervention

Overview. Using a client-centered approach, we will create a young woman-centered kit consisting of HIV self-testing, PrEP refills, STI self-sampling, and pregnancy tests and contraception (if desired), along with educational materials and kit delivery protocols for peer delivery in the community. We will hold individual interviews and focus group discussions with Kenyan women (age 16-24) in an iterative manner to optimally design *PrEP My Way* (the kit with instructional materials) and peer delivery system (including phone-based communication and kit delivery plans).

The intervention. *PrEP My Way* will be developed through an iterative, client-centered process. However, we anticipate that it will involve one clinic-based visit to safely initiate PrEP and contraception per Kenyan national guidelines [35], followed by quarterly community-based peer delivery of a pre-packaged, visually-appealing kit with pictorial and video guidance (to be

modeled after PrEP@Home, noted above). The peer delivering the kit will be trained to provide basic education (e.g., anticipated side effects) and support use of the kit components (e.g., using the HIV test, collecting the vaginal swab). The peer will also have a smart phone to show the video if the participant does not have her own smart phone. Women taking *PrEP My Way* will communicate with peers via mobile phones (e.g., SMS, WhatsApp) to arrange for kit delivery via unmarked vehicles (typically motorbikes, called "boda bodas") at home or a Safe Space (i.e., existing, designated community locations with private bathrooms, which are currently available in Kisumu through programs such as the PEPFAR-supported DREAMS initiative) during reasonable hours. Peers will not wear uniforms to avoid attention; they will also wear helmets on the motorbikes and only use pre-screened drivers for safety. Two-way mobile phone communication will also be used to convey test results and provide on-going support and empowerment. Follow-up with the clinic will occur annually and as needed (e.g., treatment for positive tests).

Kit component. We anticipate the kit will include the following elements:

- **HIV self-testing**. We will offer a choice of testing modalities. We will encourage the use of the finger prick test because of higher sensitivity; however, the oral test may be preferable to some.
  - The **AtomoRapid™ HIV Test** is an integrated HIV test of blood for the presence of antibodies to HIV-1/2. It uses a contact-activated auto-retracting safety lancet to safeguard against needlesticks and cross contamination (all material and waste are within the kit itself). AtomoRapid's interlocking features ensure each user step is performed in the correct sequence to help reduce user errors. Blood collection and delivery is controlled within the test which simplifies test procedures and improves blood volume accuracy. Testing takes ~15 minutes with a sensitivity of 99.8% and specificity of 100%.
  - The **OraQuick™ In-Home HIV Test** is the first FDA approved test (2012) that uses oral fluid to test for antibodies to HIV-1/2. The OraQuick In-Home HIV Test is a qualitative test that gives visually read results: preliminary positive, negative, or test not working (invalid) in about 20 minutes. The OraQuick oral fluid test has a sensitivity 91.7% and a specificity of 99.9%.
- **STI self-sampling for gonorrhea and chlamydia.** Women will be instructed on how to collect vaginal swabs. In brief, a cotton swab (similar to a large Q-tip) will be inserted ~5 cm into the vagina and rotated gently for ~30 seconds. This approach has been shown to be feasible and acceptable in South Africa [36] Malawi [37], and Senegal [38]. Samples will then be transported to the Lumumba Clinic for processing by GeneXpert PCR test (Cepheid).
- **Pregnancy test**
- **Contraception**
  - Oral pills (e.g., Microgynon by Bayer Pharma AG, Germany)
  - Self-injection medroxyprogesterone (by DKT, India)
  - Condoms

Other necessary testing for initiation of PrEP will not be included in the kit (i.e., creatinine and Hepatitis B), because it will be done at baseline in the clinic with PrEP initiation. An extra HIV test may be given for participants to use with their sexual partners if requested.

Design of the kit and pictorial and video guidance. We will contract with ARK, a Nairobi-based design firm, to adapt PrEP@Home specifically for young women in Kenya. ARK is a full-service design firm that has over a decade of experience throughout the region and on the global stage. Their team brings vast expertise in design research, product design, filmmaking, and visual design, as well as a nuanced understanding of sexual health interventions in Kenya specifically.

Of particular relevance, ARK has worked in Kisumu to design technology to enhance efficiency in health sector service delivery for another client; ARK will build on this experience in facilitating the design of *PrEP My Way*. ARK staff involved with the study will undergo sensitivity training, including protections for human subjects in research; confidentiality of the study participants will be particularly emphasized.

ARK will first solicit ideas from young women to produce an initial version of the *PrEP My Way* kit, pictorial and video guidance materials, and planned delivery protocol to use in the assessment process described below. They will then generate iterative versions of the kit, pictorial guidance, and video based on the feedback. The final version will be used for the pilot RCT in Aim 2.

Recruitment, consent, and enrollment. We will identify young women to participate in the development of the intervention through Lumumba Clinic and Kisumu County Hospital. Eligibility criteria will be as follows:

- Inclusion criteria
  - Young woman (age 16-24 years); we will enroll emancipated minors (e.g., those who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage, or procreation) per Kenyan national guidelines [39]) or 16-17 year-olds with parental consent
  - Reported sexual activity within the past 3 months
  - Interest in taking PrEP (actual PrEP uptake is not a requirement for Aim 1)
  - Residence in the Kisumu region
  - Phone ownership
  - Ability to understand KiSwahili, DhoLuo, and/or English
- Exclusion criteria- inability to provide informed consent (e.g., intoxication, mental disability)

Participants will be approached randomly (e.g., the second client presenting on a given day) with stratification by age (16-20 versus 20-24 years). The study will be explained to potential participants, including a complete explanation of the benefits, risks, and procedures involved. Interested women will be asked to sign an informed consent form using the language of her choice (i.e., Swahili, Dholuo, or English). All activities will be conducted in a private setting. Only one participant will be enrolled per day to avoid clustering effects, as young women often present for PrEP services in groups [40], as seen in our MPYA study. A small incentive/thank you gift (worth ~300 Kenyan Shilling or $3 US) will be provided at the time of participation; transportation will be reimbursed if needed.

If recommended by the participants, we may also conduct individual interview relevant community members for supplementary information, including clinicians, pharmacists, community organization leaders, and/or boda boda drivers. The only exclusion criterion for this group of participants would be the inability to provide informed consent (e.g., intoxication, mental disability).

Design process. Using a client-centered design approach [31] as described above, the process will begin with individual interviews (typically 1-1.5 hours in duration) based on open discussion with no mock-ups to influence (e.g., anchor) the participants' opinions (N.B., to maintain this open approach, ARK has intentionally not provided a mock up even for this protocol). Participants will have the opportunity to use each component of the kit. Our goal will be to find similarities in design preference and identify any previously missed opportunities. Individual

interviews will be utilized to avoid negative peer pressure and/or suppression of individual viewpoints. Attention will be paid to potential for stigma or other negative experiences in all aspects of the intervention. The overall guiding principal is to make *PrEP My Way* easy, engaging, and desirable for young women. Examples of solicited feedback are as follows:

1) Kit: visual appearance and size
2) Pictorial instructions: clarity of meaning, choice of cartoon figures
3) Video guidance: clarity of meaning; choice of setting, actors, music
4) Delivery protocol: peer characteristics, vehicles for delivery, setting and timing of delivery

Later interviews will include evolving mock-ups of each of the physical components of the intervention and a story board for the video. After reaching saturation (anticipated by the 15th interview), we will conduct 2 focus group discussions with up to 5 women each to assess for group dynamics that might influence the design. Interviews and focus group discussions will be digitally recorded and transcribed for analysis. They will be conducted in KiSwahili, Dholuo, and/or English per the preferences of the participants (N.B., these three languages are commonly used together in this setting and will be spoken fluently by members of the local study team); language preferences will be considered in scheduling participants together. All written materials will be available in in KiSwahili, Dholuo, and English. The video will likely be produced in a commonly used combination of English and Swahili, called “Sheng”, pending input from the participants.

Throughout this process, ARK will create a playbook (i.e., a detailed reference guide) to breakdown insights learned and explain the rationale of the process used. A workshop will also be held, involving clients, designers, and investigators together, to compile the final version of the intervention. During the workshop, participants will assume each other’s rolls to give new insights into their perspectives and needs. The final kit, pictorial instructions, and video will be produced once all input has been obtained.

Analysis. To analyze the interviews and focus group discussions, we will use a framework approach, described in Richie and Spencer [41], which involves systematic coding to identify and define concepts, map the concepts, create typologies, find associations between concepts, and seek explanations from the data. We will use Dedoose (Version 8.0.35) for coding data. Double coding will ensure that interpretations of quotes are consistent, and that data quality is rigorous and transparent; differences between coding will be resolved by discussion involving other members of the research team. Recurring issues, concepts, and patterns will be identified using both inductive and deductive reasoning. Analyses will consider whether findings differ by age and/or language.

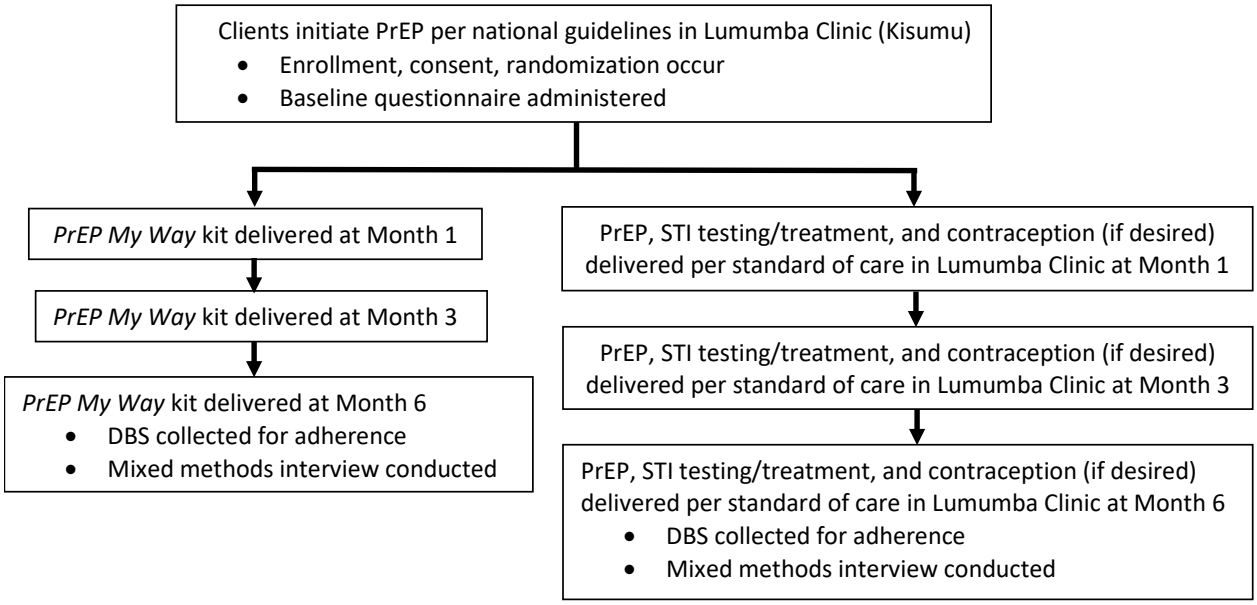
Summary/deliverable. This aim will produce a young woman-centered kit with pictorial and video guidance for peer-delivery of PrEP, STI testing, and contraception that is ready for assessment in Aim 2.

Aim 2. Assess *PrEP My Way* for feasibility, acceptability, and preliminary impact on PrEP adherence and program retention

Overview. We will randomize up to 150 Kenyan women (age 16-24) to *PrEP My Way* versus standard of care (i.e., clinic-based delivery of PrEP and sexual health services) and follow them for 6 months. Feasibility will be assessed by receipt of the kit at 1, 3, and 6 months and ability to use its components per protocol. Acceptability will be determined through a mixed-methods interview at 6 months. Preliminary impact will be evaluated by dried blood spot tenofovir levels (adherence) and kit use/clinic attendance at 6 months (retention) as primary outcomes.

Potential influencing and mediating socio-behavioral factors will be explored with questionnaires at enrollment and 6 months. See Figure 4 for an overview of the participant flow.
Recruitment. We will identify young women to participate in the pilot RCT at the time they initiate PrEP at the Lumumba Clinic or Kisumu County Hospital. Participants may also be identified in the nearby community and invited to attend either facility to initiate PrEP and enroll in the study. Community recruitment will be done in areas such as hotspots, fish landing points, and within the general low end estates with the help of community health volunteers. These participants will be distinct from those engaged in the development of the intervention (Aim 1) to increase likelihood of generalizable findings. Similar to Aim 1, participants will be approached randomly (e.g., the second client seen on a given day) with stratification by age (16-20 versus 20-24). Only up to three participant will be enrolled per site per day to avoid clustering effects, as young women often present for PrEP services in groups [40].

Figure 4. Participant flow for the pilot RCT of *PrEP My Way* versus standard of care



Consent, enrollment, and randomization. Eligibility criteria for the pilot RCT participants are as follows. All participants will have started PrEP within the past two weeks:

- Inclusion criteria
  - Young woman (age 16-24 years); we will enroll emancipated minors (e.g., those who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage, or procreation) per Kenyan national guidelines [39] or 16-17 year-olds with parental/caregiver consent
  - Initiating PrEP (this criterion subsumes all necessary safety assessments for starting PrEP, including HIV-negative status, normal renal function, and lack of Hepatitis B infection)
  - Reported sexual activity in the past 3 months
  - Residence in the Kisumu region (maximum of 20 km from our study offices at RCTP)
  - Phone ownership
  - Ability to understand KiSwahili, DhoLuo, and/or English

- Exclusion criteria- inability to provide informed consent (e.g., intoxication, mental disability)

Note: Participants may also be excluded at the discretion of the principal investigator (e.g., because of co-enrollment with a study that would compromise study aims or disruptive behavior).

Participants will be consented as described in Aim 1, enrolled, and randomized (1:1) using a computer-generated simple randomization sequence to receive *PrEP My Way* or follow up as usual at Lumumba Clinic or Kisumu County Hospital over the next 6 months. The code creating the random allocation order will be generated and maintained by the study analyst (separate from the investigators). A variable size block randomization scheme will be implemented to produce the randomization list. Randomization will be implemented by transcribing onto paper within numbered envelopes. Thus, neither participants nor study staff will be blinded to each participant's randomization arm assignment. Fidelity of randomization will be confirmed with tracking in REDCap.

Study procedures (Some aspects of the planned procedures may change pending input from Aim 1 findings). Study procedures for both arms are summarized in Table 1.

Table 1. Summary of study procedures by arm. Each cell indicates how/where the procedure will take place.

	M0	M1	M3	M6	M0	M1	M3	M6
	PrEP My Way				Control			
Education (PrEP, sexual health)	Clinic	Peer	Peer	Peer	Clinic	Clinic	Clinic	Clinic
HIV testing	Clinic	Kit	Kit	Kit	Clinic	Clinic	Clinic	Clinic
PrEP	Clinic	Kit	Kit	Kit	Clinic	Clinic	Clinic	Clinic
STI sampling	Clinic^	Kit	Kit	Kit	Clinic^	Clinic^	Clinic^	Clinic^
Pregnancy testing; contraception	Clinic	Kit	Kit	Kit	Clinic	Clinic	Clinic	Clinic
Questionnaire administration	RA	--	--	RA	RA	--	--	RA
Acceptability scale and interview	--	--	--	RA	--	--	--	--
DBS	--	--	--	RA	--	--	--	RA

Clinic=Lumumba Clinic or Kisumu County Hospital; ^STI testing done only in the setting of symptoms; RA = research assistant; time and motion studies will also be done at the KEMRI Research Care and Training Program (i.e., the study site), Lumumba Clinic, and Kisumu County Hospital mid-way through the study period

Intervention condition. A research assistant will administer a baseline demographic and socio-behavioral questionnaire (see Table 2) at enrollment (Month 0) and exchange contact information with the participant. Tentative plans will be made for the first kit delivery at Month 1. The meeting will take place at the location, date, and time preferred by the participant; we anticipate the location will be private (e.g., home or a Safe Space) and should have a bathroom to facilitate hygienic sample collection. The meeting will occur during reasonable working hours to ensure the safety and comfort of peers and participants.

Table 2. Socio-behavioral data to be collected at enrollment and 6 months

Demographics	Age, residence type (urban/rural, with family/partner), employment/education
Alcohol/substance use	Rapid Alcohol Problems Screen-4* [42], use of marijuana and other drugs
Depression	PHQ-9*^ [43]
Sexual behavior	Number, type of partners (incl. HIV status), use of condoms, transactional, intimate partner violence [Pulerwitz, PLoS One 2018]
HIV and PrEP stigma	Perceived HIV stigma scale (modified Berger, adapted for Kenya)*^ [44]; PrEP stigma scale [45]#
Belief in PrEP	Knowledge about reduction in HIV risk due to PrEP, Belief in Medicines Questionnaire*^ [46]
Self-esteem/efficacy	Rosenberg Self-Esteem Scale*^ [47]

Empowerment	Modified Sexual Relationship Power Scale [48]*^
Clinic satisfaction	Patient-Healthcare Provider Relationship [Stall, JAIDS 2006]#

* validated, ^utilized previously in Kenya, #this scale will be exploratory as it has not yet been used in the population

At kit delivery, the peer will guide the participant through the pictorial materials for each aspect of the kit and show her the video. HIV test results will be available at the time of testing. The peer can be present to see the test results or not, per the participant's preference. She will answer any questions regarding the kit and its components; any challenging questions will be brought back to clinical staff at the RCTP study site and answers relayed to the participant via phone. The peer may also provide weekly empowerment messages (e.g., "Remember- PrEP gives you control over your sexual health") via phone; participants will be able to opt out of these messages, if desired (e.g., for privacy). The peer will obtain the HIV test results and document PrEP and contraception use. She will bring the vaginal swab back to the study site for processing. The peer will also dispose of any remaining materials, if desired by the participant. The peer will send an SMS or WhatsApp message indicating either normal results or the need for the participant to come to the study site for abnormal or indeterminate results within a few days. Explicit mention of STI testing will not occur in the messages to protect the participant's privacy of the participants. Treatment and supportive counseling will then be provided by our staff per Kenyan national guidelines [35]. Arrangements will be made for prompt repeat HIV testing at our study site if any of the self-testing kits reveal a positive or indeterminant result; linkage to free antiretroviral therapy services will be facilitated in the event of a confirmed seroconversion. Participants will be offered repeat STI testing in the clinic if their self-collected samples are inadequate for testing. Follow-up for any other concerning situations (e.g., social harms) will be arranged by study staff as appropriate (see *Human Subjects*).

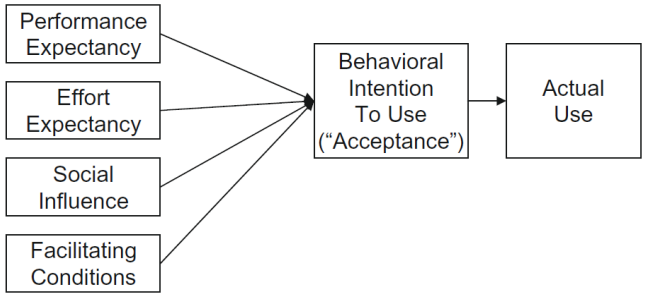
At completion of the visit, the peer will make tentative plans for a repeat visit in two months (Month 3 of PrEP). She will remind the participant that she is available via mobile phone for any *PrEP My Way*-related questions and support. She will then contact the participant one week in advance of the tentative visit appointment to confirm it or make any necessary adjustments. Scheduling will aim to avoid any lapses in PrEP coverage and will occur in a private location during reasonable working hours, as described above.

The above-noted procedures will be repeated at the Month 3 and Month 6 visit. Additionally, at the Month 6 visit, an RA will collect the following data either in the field or at the study site (within the next two weeks):

- Dried blood spot for tenofovir concentration
- Creatinine (point-of-care)
- Socio-behavioral data (quantitative questionnaire; see Table 1)
- Acceptability data (see below)

Acceptability will be determined quantitatively with the Systems Usability Scale (SUS; [49]. This 10-item Likert scale assesses domains including desired frequency of use, complexity, need for support, functionality, irregularities, ease of learning/use, time required for use, confidence, and training needed. Qualitatively, we will explore *PrEP My Way* in accordance with the Unified Theory of Acceptance and Use of Technology (UTAUT; Figure 5) in up to 20 participants purposively selected to

Figure 5. Unified Theory of Acceptance and Use of Technology



reflect high and low usage of the kits. Questions for each model component are described in Table 3.

All quantitative data will be recorded on encrypted tablets in REDCap. Qualitative interviews will be digitally recorded and transcribed. All data will be collected in a private space using the participant's preferred language (KiSwahili, DhoLuo, or English).

Table 3. Questions to be used in assessing *PrEP My Way* acceptability

Model component	**Question content**
Performance expectancy	Perceived usefulness, personal outcome expectations
Effort expectancy	Perceived effort needed to arrange delivery and use the kit components
Social influence	Perceived norms and stigma
Facilitating conditions	Kit delivery, instructional materials, role of the peer
Behavioral intention to use	Attitudes around current and anticipated future use/non-use
Actual use	DBS tenofovir concentration

Participants will then be disenrolled from the study and linked back to the Lumumba Clinic, Kisumu County Hospital, or a similar clinic of their choice, for continuation of PrEP as desired. A small incentive/thank you gift (worth a minimum of ~500 Kenyan Shilling or $5 US) will be given at that time for transport and completion of study-related activities (not *PrEP My Way* utilization). The estimated time spent with the participant will be ~2 hours at enrollment, 30 minutes at Months 1 and 3, and ~1 hour at Month 6.

Control condition. After randomization, a study research assistant (RA) will administer the baseline demographic and socio-behavioral questionnaire. Control participants will then continue to receive PrEP and any other desired sexual health services at Lumumba Clinic or Kisumu County Hospital. The study may provide or assist the clinics in obtaining necessary supplies for routine HIV/STI services in the event of supply chain stock outs. The RA will call the control participant in ~3 months to maintain accurate contact information and remind her that the RA will meet her at her 6-month PrEP appointment in the Lumumba Clinic or Kisumu County Hospital for the final study visit. The RA will make a reminder call one week in advance. If the control participant does not wish to continue PrEP or return to the Lumumba Clinic/Kisumu County Hospital, she may come to the RCTP study site for the final study procedures. The RA will then collect the following using the methods described above:

- Dried blood spot for tenofovir concentration
- Socio-behavioral data (quantitative questionnaire)
- Review of Lumumba Clinic/Kisumu County Hospital chart records for HIV and STI testing and pick up of PrEP and contraception; participants may be asked for clarification if chart records are incomplete

Control participants will then be disenrolled and provided with a small incentive/thank you (worth at least~500 Kenyan Shillings or $5 US) for completion of study-related activities. They will continue to receive PrEP and other sexual health services at Lumumba Clinic, Kisumu County Hospital, or another clinic as desired.

Peer identification and hiring, and oversight. Peers will not be participants. They will be identified from PrEP programs in the Kisumu region. Peers will be 18-30 years old women who have themselves taken PrEP for at least 3 months and are fluent in KiSwahili, DhoLuo, and/or English. If they do not own a smart phone, the study will provide one for showing the *PrEP My Way* video guidance and enabling two-way communication with participants (e.g., SMS, WhatsApp). Although already experienced with PrEP, all peers will be trained about PrEP using Kenyan national guideline materials [35]. They will also undergo sensitivity training, including

protections for human subjects in research; confidentiality of the study participants will be particularly emphasized. Peers will receive a stipend of 20,000 Kenyan Shillings (~$200 US) per month, consistent with payment for peer/lay healthcare workers in other community-based health programs in the area. We will recruit three peers with each serving 15-20 participants. With the projected enrollment schedule over three months and the quarterly follow-up, this case load will amount to 8-16 clients per month, or 1 delivery every 1-2 work days (assuming ~20 work days per month). This workload is reasonable, even if multiple attempts are needed to successfully deliver the kit. Participants will have options for engaging with peers, ranging from none beyond kit delivery to step-by-step support in using each component of the kit and follow-up questions by phone.

We will document the training process for the peers to promote reproducibility in future studies and/or program implementation.We will also observe the quality of the peer's engagement with participants to document the content of their interactions, which can be accomplished during the planned time and motion studies (below).

Cost. Because intervention effectiveness is not the aim of this study, we will not perform a formal cost-effectiveness analysis. However, we will collect costing data on the components of the intervention and perform time and motion studies over two-week periods in both the intervention and control arms of the study mid-way through the study period (i.e., when procedures are running smoothly). Up to 20 client interactions will be observed in each setting to capture the range of time and extent of effort required for PrEP, contraception, and STI services. An RA may observe the peers working with participants in the community, or the peer may perform the observation herself (per the preference of the participant). No identifiers of specific clients in the clinic will be recorded. This data will be used to formulate a preliminary sense of the costs of the *PrEP My Way* intervention relative to standard of care.

Outcome measures

Feasibility. Feasibility will be assessed by the following metrics: 1) receipt of the *PrEP My Way* kit at Months 1, 3, and 6, and 2) ability of the participant to use each aspect of the kit (i.e., the HIV self-test, use of the vaginal swab, and self-administration of medroxyprogesterone [if desired]) per protocol. The intervention will be considered feasible if ≥70% (35/50) participants 1) receive a kit and 2) achieve a readable HIV test, usable vaginal swab, and self-injection of medroxyprogesterone, if desired, at ≥66% (2/3) of visits.

Acceptability. The PrEP My Way intervention will be considered acceptable if >70% (35/50) participants rate 70% (7/10) items on the SUS as "very good" or higher. The qualitative interview will delve deeply into each of the four domains of the UTAUT model to provide in depth feedback on the intervention.

Primary outcomes- Preliminary impact on PrEP adherence and program retention at 6 months. PrEP adherence will be assessed primarily by DBS for tenofovir diphosphate (TFV-DP) concentration. The TFV-DP concentration will provide an estimate of doses taken over the prior 3 months (see Table 4; [11, 50]). Retention will be assessed by kit receipt in the intervention arm and clinic attendance per clinic records in the control arm at Month 6. Potential influencing and mediating socio-behavioral factors (Table 2) will be explored.

Secondary outcomes. We will assess the following:

Table 4. TFV-DP concentrations in DBS	
Estimated use	Median fmol/punch (IQR)

- Self-reported PrEP adherence at Months 1, 3, and 6 (intervention arm) and Month 6 (control arm). We will use the 3-item scale developed by Wilson et al, which involves different recall tasks (frequency, percent, and rating of adherence) over the prior 30 days [51]

Protective*	>1,250
Moderate	900-1,249
Low	<900

*Exact value to be explored (see text)

- PrEP persistence over the 6-month period
- Rates of STI testing at Months 1, 3, and 6
- Rates of pregnancy test and contraception pick up at Months 1, 3, and 6
- Cost estimates

Analysis

Feasibility and acceptability. Feasibility metrics and the quantitative assessment of acceptability will be analyzed descriptively. We will use a content analysis approach to assess the qualitative acceptability data. Content analysis refers to systematic process for interpreting the content of textual data through coding and category construction [52]. We will develop a coding scheme through initial review of a randomly selected subset of 33% of interview transcripts. Sections of the transcripts that appear to address concepts of analytic interest (e.g., device design, stigma) will be assigned descriptive labels, or codes. Operational definitions will be developed for the codes to create a codebook, which will be used to code the data. We will use Dedoose software (version 8.0.23). We will then repeatedly sort and review codes to identify a broader set of concepts (e.g., social influences). The categories will be constructed from this second set of concepts by assignment of descriptive labels, formulation of operational definitions, and selection of illustrative citations from the data. We will review categories and summarize acceptance in the final, interpretive step of the analysis.

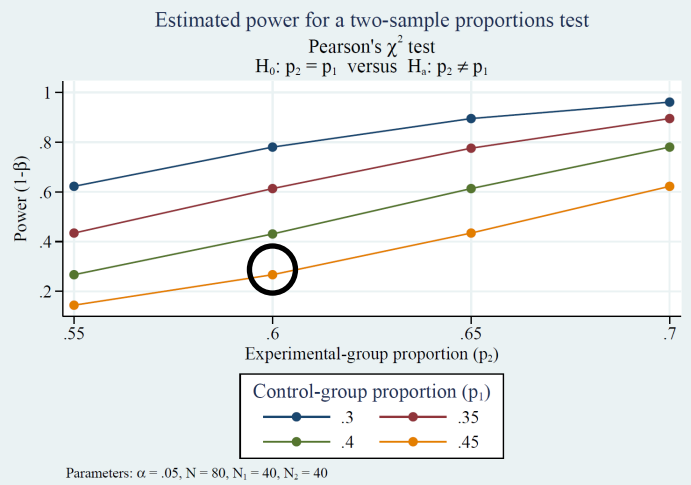
Primary outcomes. *Adherence* (as determined by TFV-DP concentrations in DBS) and program retention at 6 months will be analyzed descriptively and then compared between the two study arms using Chi-square tests (i.e., comparing protective TFV-DP concentrations versus not; retained versus not). DBS will be shipped to the University of Cape Town in South Africa and some will be tested to measure TFV-DP concentrations. We will use an intention-to-treat approach for the primary outcomes but will also perform per protocol analysis. Because of the develop-mental nature of this R34 study and the small sample size, we will assess potential influencing factors on adherence and retention using logistic regression models. Thresholds from protective TFV-DP concentrations may be explored, as this is an active area of research [53, 54]. We will pre-specify variables to avoid overfitting the models as age, self-esteem, empowerment, stigma, depression, and alcohol/substance use. We will analyze study outcomes by peer to look for any clustering effects. We will also explore empowerment and depression as mediators of the relationship between the *PrEP My Way* intervention and adherence and retention outcomes, using the approach by Valeri and VanderWeele, which allows for logistic modeling, and sensitivity analyses around key assumptions per Imai.[55].

Secondary outcomes. We will use descriptive statistics to understand self-reported adherence, PrEP persistence, early retention, and rates of STI testing, pregnancy testing, and contraception pick up. We will also explore trends for self-reported adherence within the intervention group with regression analysis. We will compare all secondary outcomes between intervention and control arms with Chi-square tests (categorical variables) and t-tests (continuous variables). As described above, we will also explore in the influence of age, self-esteem, empowerment, stigma, depression, and alcohol/substance use on any observed differences through logistic and linear regression models, for dichotomous and continuous variables, respectively.

Cost analysis will follow the Clinton Health Access Initiative guidelines for costing HIV interventions [56, 57] and will reflect the provider perspective. We will conduct activity-based micro-costing to estimate the costs of the *PrEP My Way* intervention; data will be collected from the study budget, clinic expense reports, published information on labor costs, and staff interviews. These data will be used to complete cost worksheets. Costs will be categorized as fixed or variable. Variable costs indicate which costs could change (e.g., using free communication instead of standard telephone rates) and influence the estimates from the study.

Power. We are estimating the power of the study sample based on PrEP adherence at 6 months. Based on prior studies (see Figure 2), we anticipate a 60% overall decrease in PrEP adherence from enrollment to Month 6. We estimate ~1/3 of that decrease will be due to appropriate rationale (e.g., no longer at risk for HIV acquisition or use of other HIV prevention methods such as condoms), in accordance with the concept of prevention-effective adherence [58]. We therefore believe 2/3 of a 60% decrease or 40% decrease is an ideal target for this intervention. Of note, with prevention-effective adherence, PrEP adherence should be aligned with risk for HIV acquisition and lack of use of other effective means for HIV prevention. In this study, we will be following clients for the first six months of PrEP use. We are considering this period as a "season of risk" based on the client's desire to initiate PrEP and will include the full six months in the denominator when calculating adherence and persistence. Future studies of *PrEP My Way* will include metrics of risk to determine prevention-effective adherence. We will, however, follow sexual behavior and reported risk to track the ongoing need for PrEP as a secondary analysis.

Figure 6. Estimate power for the study sample size



Our power calculations are based on 80 participants, given an expected loss to follow-up of 20% (estimated from our current MPYA study). As shown in Figure 6, assuming a standard deviation of 10%, 80 participants will have limited power to detect a difference of 20% between the study arms (e.g., ~40% power if the primary outcome is seen in 40% of the control group versus 60% in the intervention group; see the circled green dot). If a stronger effect is seen (e.g., closer to the ideal target of 40%), we may achieve >80% power. We believe this sample size is appropriate for the development of the *PrEP My Way* intervention. If the intervention is also found to be feasible and acceptable, we look forward to fully testing the intervention in a subsequent, fully powered study.

Participant retention and withdrawal

Participants will be tracked primarily through peers (intervention) and the clinic visits (standard of care). Individuals missing scheduled appointments will be contacted through study retention teams. Participants will be able to withdraw from the study at any time.

Ethical Considerations

Human subjects

This study will involve young Kenyan women in two sets of study procedures to develop and preliminarily test the *PrEP My Way* intervention.

- Intervention development (Aim 1). We will use a client-centered approach, involving individual interviews and two focus group discussions with up to 25 Kenyan women to optimally design the *PrEP My Way* kit (with instructional materials) and peer delivery system (including communication and kit delivery plans).
- Pilot randomized controlled trial (Aim 2). We will randomize 150 Kenyan women to *PrEP My Way* versus standard of care (i.e., clinic-based delivery of PrEP and sexual health services) and follow them for 6 months. These participants will be distinct from those participating in the intervention development aspects of the study. Feasibility will be assessed by receipt of the kit at 1, 3, and 6 months and ability to use its components per protocol. Acceptability will be determined through a mixed-methods interview at 6 months. Preliminary impact will be evaluated by dried blood spot tenofovir levels (adherence) and kit use/clinic attendance at 6 months (retention) as primary outcomes. Mediators and moderators of PrEP use (e.g., empowerment and mental health) will be explored through questionnaires at baseline and 6 months.

Inclusion of emancipated minors

Per Kenyan national guidelines, 16 and 17-year old girls are considered to have reached the age of majority if they have been pregnant or diagnosed with an STI. They will therefore not require parental/guardian consent to participate in this study. As described below, study staff will host community events and meet with a community advisory board to allay potential concerns about studying sexual health in a young population.

Pregnancy

Available human and animal data suggest that tenofovir/emtricitabine does not increase the risk of major birth defects overall compared to the background rate [59]. Moreover, Kenyan national guidelines approve the use of PrEP during pregnancy. We will therefore not limit or change participation with regards to pregnancy. All pregnant participants will be encouraged to see appropriate pregnancy-related care through the Kenyan national healthcare system.

Source of materials, recruitment of subjects and informed consent

We will obtain institutional review board approval for this study through the Kenya Medical Research Institute and Partners HealthCare/Massachusetts General Hospital. Applications will cover recruitment, written and informed consent, enrollment, data collection, retention, study procedures, protection from risk, data safety, monitoring, and analysis.

The study will recruit from the Lumumba Clinic and Kisumu County Hospital in Kisumu, Kenya, both of which has extensive experience with studies on HIV prevention and sexual health, including PrEP, STI testing, and contraception delivery, for young women. Study staff work closely with the community to provide informational sessions about all research activities, including drama activities in marketplaces, drama and interviews on radio stations, and activities as part of community events promoting HIV testing, treatment, care, and prevention.

Written consent will be obtained for the prospective implementation of all study activities. The consenting process will take place in a private room and the consent form will comprehensively provide the following information: (a) introduction to the consent process, explaining the consent form and compliance with institution policy and country laws; (b) emphasis that participation is voluntary; (c) nature and purpose of the study; (d) explanation of study procedures; (e) potential discomforts and risks, as well as plans to protect participants from these risks; (f) potential benefits; (g) alternatives to participation in the study; (h) confidentiality, including how data will

be used and how it will be kept private; (i) refusal/withdrawal, including right to withdraw consent and leave the study at any time; and (j) rights and complaints. After each major section, research staff obtaining consent will pause and check for understanding -- for example, by asking the potential participant to repeat, in their own words, what "the right to refuse" means.

All recruitment, consent, and enrollment procedures, as well as all study procedures, will be conducted in the participant's preferred language (i.e., Swahili, Dholuo, or English).

Potential risks and protection against risk

Study participants will face the following risks from the study procedures:

1. Risk: Taking PrEP may be associated with some health risks. PrEP (300mg tenofovir, 200mg emtricitabine) will be initiated in Lumumba Clinic and Kisumu County Hospital per Kenyan National Guidelines. It will be continued through those clinics for participants in the control arm and provided through the RCTP (study site) for those in the intervention arm. Risk communication about PrEP through study staff will be consistent Kenyan National Guidelines, which are also consistent with World Health Organization guidelines. In brief, mild side effects may occur in as many as 1 out of 10 people and include mild kidney function (only detected by laboratory tests), fatigue, upset stomach, vomiting, loose stools, and dizziness. More severe side effects are rare and may occur in less than 1 out of 100 people; these include rash, liver function problems, serious kidney damage and allergic reaction. Small changes in bone strength have been observed, but not associated with any fractures or symptoms. PrEP may interact with some other medications.
   Protection: Safety for PrEP initiation (e.g., HIV, creatinine, and Hepatitis B testing) will be performed at Lumumba Clinic/Kisumu County Hospital prior to enrollment in this study. For intervention participants, HIV testing will be provided with all *PrEP My Way* kits prior to PrEP refill, and creatinine will be tested at 6 months by the study staff at Lumumba Clinic/Kisumu County Hospital to evaluate kidney function. For control participants, HIV and creatinine testing will be available per Kenyan National Guidelines at routine follow-up visits. Participants will be advised to call or come to the study clinic if they have unexplained increased or decreased urination, weight loss, cramps, muscle pain, dizziness, excessive fatigue, nausea, vomiting, or shortness of breath. Study staff will be available 24 hours a day/7 days a week to evaluate potential side effects from taking PrEP. A medical officer from the study team will perform any necessary examinations and determine if PrEP should be stopped and/or if further testing and care is needed. Participants will also be advised on potential drug-drug interactions.

2. Risk: HIV acquisition and drug resistance may occur during study follow-up if a participant acquires HIV in spite of PrEP use, or during a break from PrEP and thereafter resumes PrEP.
   Protection: Per Kenyan national guidelines, participants in both study arms will receive standard counseling about HIV prevention through means other than PrEP (i.e., condoms, sexual partner reduction, and use of ART in any sexual partners who have HIV infection). Condoms will also be available free-of-charge. HIV testing will be performed prior to each disbursement of PrEP, as described above. Such frequent testing will decrease the potential for drug resistance to develop in the setting of acute HIV infection. If HIV seroconversion does occur, we will provide counseling for potential emotional trauma and assist with linkage to HIV treatment and care programs, which are widely available and free-of-charge through the Kenyan national healthcare system.

3. Risk: Privacy may be lost through use of the *PrEP My Way* kit.
   Protection: We will advise participants on the potential for kit delivery to attract attention. We will minimize this risk by using unmarked vehicles (typically motorbikes that are commonly used for routine, day-to-day activities) and making deliveries at the preferred date, time, and location of the participants. Peers will also not wear uniforms, and they will be trained in human subjects protections, with emphasis placed on the importance of privacy and confidentiality. All samples will be labeled with the participant's unique study ID number and date. This information will only be linked to identifiable information (e.g., the participant's name) in databases that are stored securely with encryption and password or in locked cabinets (as described in the protocol). Samples will be transported in unmarked bags that will not indicate the name of the study, participants, or staff. Text and WhatsApp messages will not explicitly mention STI tests to protect the participant's privacy of the participants.

   We will hire three peers to work with study participants. We believe the likelihood of a participant knowing all three is low. However, if she does know all the peers, she can decide to continue or not with study participation. We will also give each participant the option of changing peers at enrollment or during the course of the study per her preference (e.g., in case of interpersonal conflict).

4. Risk: Emotional discomfort, physical discomfort, bleeding, or rarely infection may occur from HIV self-testing, vaginal swab self-sampling for gonorrhea and chlamydia testing, and/or self-injection of medroxyprogesterone.
   Protection: All self-administered components in the *PrEP My Way* kit are licensed for routine clinical use and are generally considered safe. We will promote emotional and physical comfort with these components through client-centered design of all pictorial and video guidance. Peers will also be trained to support their use in person at the time of kit delivery, as well as through mobile phone interactions (e.g., SMS, WhatsApp).

   Group chats will be voluntary and participants will be informed of their right to opt out of them if they have any privacy or confidentiality concerns. This approach has worked well within the POWER study (conducted by Drs. Bukusi and Baeten) in the same study setting with no concerns reported. The WhatsApp or text messages between the peer and the participant will be closed (i.e., meaning no other individuals will be included). Peers will use password protected, encrypted phones to prevent loss of privacy/confidentiality and will receive training on the importance of privacy/confidentiality as noted above. Participants will be encouraged to use passwords on their personal phones and delete any message they do not want seen by others.

5. Risk: Privacy may be lost through security breaches with data collected through the study.
   Protection: All consent forms will be stored in locked cabinets at the research sites. All electronic data from interviews, focus group discussions, questionnaires, and test results will be stored securely on encrypted, password-protected devices and in REDCap (hosted at MGH), which is in compliance with HIPAA standards.

6. Risk: Some participants may experience fatigue from completing study interviews, focus group discussion, and/or questionnaires.
   Protection: We will keep all study procedures as short as possible to minimize the risk for fatigue. We will also allow participants to take breaks when needed.

Potential benefits and relation to risks
During the study, participants will receive the same services available to them through the routine Kenyan healthcare clinics: HIV testing, PrEP, STI testing/treatment, pregnancy tests, and contraception. Participants in the intervention arm will have the added benefit of service delivery and peer support. All participants will receive an incentive (300 Kenyan Shillings, ~$3) for their time at enrollment and the 6-month follow-up visit.
We feel the risks associated with the study are small. The benefits are consistent with cultural expectations and they follow the established standard with institutional review board approval in our other studies (e.g., MPYA as described above). We therefore believe the balance of benefit and risk is appropriate.

Expected Application of the Results
High persistent adherence and program retention are critical for achieving HIV prevention from PrEP, but are currently limited for young women in sub-Saharan Africa by stigma and structural barriers. *PrEP My Way* is a theory-based intervention to overcome these barriers and empower young women to achieve the benefits of PrEP, as well as STI management and contraception. This study will determine if *PrEP My Way* is feasible, acceptable, and likely to have impact on PrEP adherence and program retention. This knowledge is a critical step toward full testing of the intervention in a future R01 grant. If successful, *PrEP My Way* could help support the HIV prevention and sexual health needs of the millions of young women in the “youth bulge” that will affect Africa in the coming decade.

Community advisory board (CAB)
Lumumba Clinic maintains an active community advisory board with ten standing members representing the surrounding Kisumu region, as well as capacity for rotating members depending on the needs of each study. For this protocol, the CAB will be enriched with two young women taking PrEP. The study will be presented during the protocol development phase and at least annual thereafter for feedback and guidance on both implementation of study procedures and interpretation and dissemination of findings.

Data and safety monitoring plan
Drs. Haberer and Bukusi will work closely together to ensure that high quality data is collected and the safety of study participants is upheld. Dr. Bukusi will be responsible for oversight of the day-to-day activities in Kisumu. Drs. Haberer and Bukusi will communicate approximately weekly (e.g., by Skype/Zoom) with email more frequently as needed. Drs. Haberer will visit the site twice annually, and Drs. Siegler and Baeten will visit at least annually, to facilitate study operations, including trainings, monitoring, evaluation, and result dissemination. Reports on study progress will be generated at least monthly and shared among the investigators for discussion. Dr. Bukusi will communicate any adverse events to Dr. Haberer within 72 hours; all serious adverse events will be reported to the KEMRI and MGH institutional review boards according to their requirements (generally 7 days).

ClinicalTrials.gov requirements
Dr. Haberer will be responsible for registering and providing updated information about the clinical trial on ClinicalTrials.gov.

Treatment for Injury
Participants will be asked to inform the study staff if they feel they have been injured because of taking part in the study. Injuries may also be identified during laboratory testing, medical histories, and physical examinations. Treatment for adverse events related to study participation

will be provided by the study clinic at RCTP. If treatment is required that is beyond the capacity of the study clinic, the study doctors will refer the participant to appropriate services or organizations that can provide care for the injury.

Study Records
Site Investigators will maintain, and store in a secure manner, complete, accurate, and current study records throughout the study. The investigator will retain all study records for at least seven years after completion of the study. Study records include administrative documentation and regulatory documentation, as well as documentation related to each participant screened and/or enrolled in the study, including informed consent forms, questionnaires, notations of all contacts with the participant, logs linking participant name to study identification number and other identifying information in study files, and all other source documents. After seven years, these documents may be destroyed.

Participants' study information will not be released without their written permission, except as necessary for oversight by:

- Study investigators
- Study funders
- Site institutional review boards
- Massachusetts General Hospital
- Kenya Medical Research Institute

Investigator roles
Dr. Haberer will be the overall PI for the study; she will be responsible for development of the study protocol, training and data collection materials, domestic regulatory approval, data management systems and quality control, data analysis, manuscript preparation, and result dissemination.

Dr. Bukusi will serve as the site PI for the study; she will provide significant input on the study protocol, training and data collection materials, data analysis, manuscript preparation, and result dissemination. She will also oversee day-to-day staffing needs and data collection activities.

Dr. Siegler serve as a co-investigator and will provide significant input on the design and use of the *PrEP My Way* kit, building on his experience with a similar intervention for men who have sex with men in the US. He will also assist with data analysis, manuscript preparation, and result dissemination.

Dr. Baeten will be a consultant for this study, providing input regarding the protocol, analysis, manuscripts, and other dissemination activities. He has a well-established relationship with Drs. Haberer and Bukusi and will be readily available for consultation.

Dr. Haberer will host monthly investigator calls to review study activities and facilitate input. She will also organize longer semi-annual meetings to reflect on study progress and impact; every other meeting will be held in Kenya. All investigators will be in regular communication via email.

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