

Peer PrEP referral + HIV self-test delivery for PrEP initiation
among young Kenyan women: Pilot study & randomized
implementation trial

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Protocol

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1011 **Peer PrEP referral + HIV self-test delivery for PrEP initiation**
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132 ABBREVIATIONS

133	3TC	Lamivudine
134	AE	Adverse Event
135	AGYW	Adolescent girls and young women
136	ART	Antiretroviral Therapy
137	DAIDS	Division of AIDS (NIH)
138	DBS	Dried Blood Spots
139	EC	Ethics Committee
140	FDA	Food and Drug Administration (US)
141	FGD	Focus Group Discussion
142	FSW	Female sex worker
143	FTC	Emtricitabine
144	FTC-TP	Emtricitabine-triphosphate
145	HCW	Healthcare worker
146	HIVST	HIV Self-testing
147	IEC	Information, communication, education
148	IRB	Institutional Review Board
149	KEMRI	Kenya Medical Research Institute
150	MoH	Ministry of Health
151	MSM	Men who have sex with men
152	NGT	Nominal group technique
153	NIH	National Institutes of Health (US)
154	PHRD	Partners in Health & Research Development
155	PrEP	Pre-exposure prophylaxis
156	RA	Research assistant
157	SAE	Serious adverse event
158	TDF	Tenofovir
159	TFV-DP	Tenofovir diphosphate
160	UNAIDS	Joint United Nations Program on HIV/AIDS
161	WHO	World Health Organization
162	NASCOP	National AIDS and STIs Control Programme
163		

164

PROTOCOL SUMMARY

165 Pre-exposure prophylaxis (PrEP) for HIV prevention is highly effective. In Kenya, a country with the 4th
166 largest HIV epidemic worldwide, the government began delivering PrEP on a national scale in 2017. One
167 of the target groups for HIV incidence reduction is young women (16-24 years), who account for 33% of
168 the total of new HIV infections in Kenya yet comprise only 10% of the population. To date, PrEP initiation
169 rates are low among young women. Barriers to PrEP initiation are multi-faceted and include institutional
170 (e.g., stigma associated with use), and intra-personal (e.g., lack of PrEP knowledge or self-efficacy)
171 barriers. Thus, innovative PrEP delivery models that can help overcome these barriers – and that are
172 affordable to young women and health systems – are needed.

173 The opinion of peers often influences the behaviors and preferences of young women, globally and in
174 Kenya, including opinions related to health and health care. Peer referrals or peer-delivered interventions
175 have been commonly used among key populations with tight social connectivity to increase identification
176 of new individuals living with HIV and facilitate linkage to treatment but have not yet been used to increase
177 identification of individuals eligible for HIV prevention and facilitate linkage to interventions like PrEP. We
178 hypothesize that a formalized peer PrEP referral + HIVST delivery model can amplify screening for HIV
179 and PrEP initiation among young Kenyan women at HIV risk. Specifically, this study aims to:

180 **Aim 1: Pilot and refine a peer PrEP referral + HIVST delivery model**

181 Approach: Pilot the aim 1 delivery model among 16 young female PrEP users in Thika, Kenya, who will
182 deliver formalized peer PrEP referral + HIVSTs to ~4 peers each (=64 peers total). One month later, we
183 aim to measure model adoption (e.g., peer referral, HIVST use, and PrEP initiation) through quantitative
184 measures. We also aim to understand model acceptability and model weak points for refinement through
185 qualitative data collection using CFIR-informed focus group discussions (FGDs) with those delivering and
186 receiving the intervention (4-5 FGDs, 3-6 participant/FGD).

187 Hypothesis: *The proposed model will be adopted and accepted by PrEP users and peers, feasible, and
188 easily refined to address identified weak points.*

189 **Aim 2: Conduct a hybrid effectiveness-implementation randomized trial to test the effect of the
190 refined peer PrEP referral + HIVST delivery model on PrEP initiation among young Kenyan women**

191 Approach: Conduct a 2-arm trial in Thika, Kenya where ~80 young female PrEP users are randomized
192 to: (1) “formal peer PrEP referral + HIVST delivery”, where they are encouraged to refer 4 peers using
193 PrEP materials (developed in Aim 1) and distribute HIVST kits (2/peer, = 8 total), vs. (2) “informal peer
194 PrEP referral”, where they are encouraged to refer 4 peers to PrEP services by word-of-mouth, as is
195 ongoing in Kenya. All outcomes will be measured among peers and PrEP users three months later.
196 Outcomes will include adoption (e.g., PrEP referral, PrEP retention, HIVST use), fidelity, cost, and safety.
197 The effectiveness outcome will be PrEP initiation (primary), confirmed using dried blood spots.

198 Hypothesis: *The formal referral model will result in higher PrEP adoption (e.g., initiation and retention)
199 among peers compared to the informal referral model and will have low cost and high fidelity.*

200 This study will provide important information on how to increase PrEP initiation among young Kenyan
201 women at high HIV risk and will inform a future proposal for a community-randomized trial that tests the
202 peer PrEP referral + HIVST delivery model at scale.

204

LAY SUMMARY

205 Few young women at risk of HIV infection are initiating pre-exposure prophylaxis (PrEP) for HIV
206 prevention in Kenya, thus we propose developing, refining, and testing a new model to increase PrEP
207 initiation among young women at high HIV risk that has not yet been explored: peer PrEP referral + HIV
208 self-testing (HIVST) delivery. Through a pilot based on qualitative formative research and stakeholder
209 engagement, we will develop and refine an acceptable and feasible model where young (≥ 16 to 24 years)
210 female PrEP users refer their peers to PrEP using materials we determine to be appropriate (e.g.,
211 pamphlets) and HIVSTs. We hypothesize that relative to informal word-of-mouth peer PrEP referral
212 (ongoing in Kenya), formalized peer PrEP referral + HIVST delivery will increase PrEP adoption (i.e.,
213 initiation, retention, and adherence) among peers, and be low cost and have high fidelity in Kenya.

214

ABSTRACT

215 PrEP for HIV prevention is highly effective. However, in Kenya, where the government offers PrEP free
216 of charge, few young women (16-24 years old) at high HIV risk are initiating PrEP. We propose piloting
217 and testing an innovative model that might overcome barriers to PrEP initiation among young Kenyan
218 women: peer PrEP referral + HIVST delivery. The specific aims of the proposed research are to: 1) pilot
219 a delivery model based on formative research and refine the model using focus group discussions
220 informed by implementation frameworks (Year 1 and 2) test the effect and implementation of the refined
221 delivery model on PrEP initiation and other outcomes (including PrEP adoption, model fidelity, and costs)
222 using a hybrid-randomized implementation trial (Years 2-3). This proposed research addresses one of
223 the greatest challenges to PrEP scale-up today and will inform a National Institutes of Health (NIH) R01
224 proposal for a community-randomized trial and budget impact analysis.
225

226 **BACKGROUND**

227

228 **Importance of the problem**

229 More than two million persons become newly infected with HIV each year, the majority in Africa.¹ In
230 Kenya, more than 1.5 million people are living with HIV² making it the country with the 4th largest
231 epidemic. The past five years have witnessed major strides in the development of highly effective HIV
232 prevention interventions, particularly using antiretroviral medications: antiretroviral therapy (ART) to
233 decrease infectiousness and pre-exposure prophylaxis (PrEP) to prevent acquisition. Novel models to
234 deliver these strategies successfully and efficiently, at scale, are needed to achieve maximum HIV
235 prevention impact.

236 **Young Kenyan women are at high risk of HIV**

237 Kenyan adolescent girls and young women (AGYW) remain at particularly high risk of HIV infection.
238 AGYW ages 16-24 years accounted for 33% (n= 23,312) of total new HIV infections in 2015, thereby
239 being nearly twice as likely to acquire HIV compared to their male counterparts.³ This discrepancy is
240 associated in part with perceptions of HIV risk, lack of knowledge and/or access to effective HIV
241 prevention interventions, and high prevalence of experienced sexual violence^{4,5} – it is estimated that 33%
242 of young women in Kenya have been raped before the age of 18 years.⁶

243 **PrEP is an effective, recommended, and impactful strategy for HIV prevention**

244 PrEP has been demonstrated to be efficacious and safe for reducing HIV risk among men who have sex
245 with men (MSM),⁷ heterosexual men and women,^{8,9} and injection drug users¹⁰ in diverse geographic
246 settings. In 2012, the U.S. Food and Drug Administration (FDA) approved combination tenofovir
247 disoproxil fumarate/emtricitabine (TDF/FTC) as the first medication with a label indication for HIV
248 prevention in adults¹¹. In 2015, the World Health Organization (WHO) issued guidance recommending
249 TDF-containing PrEP as an additional prevention option for all persons at high risk for acquiring HIV¹²
250 and in 2017, Kenya added PrEP to its national HIV prevention portfolio and began distributing free
251 government-issued PrEP to all individuals at HIV risk at select public clinics.^{13,14}

252 Adherence is essential for PrEP efficacy. PrEP clinical trials had a wide range of results for estimates of
253 PrEP's efficacy for HIV protection – explained by the degree to which the trial populations were adherent
254 to PrEP¹⁵. Secondary analyses from clinical trials and demonstration studies have shown that PrEP is
255 highly efficacious and safe when taken as prescribed: at the individual level, HIV protection is on the
256 order of 90-100% in both MSM and heterosexual populations when PrEP adherence was high, as
257 measured by the presence and quantity of PrEP in blood samples.^{8,16,17} PrEP adherence and HIV
258 prevention effectiveness have been higher than in prior clinical trials, in many cases very high, in open-
259 label demonstration projects among HIV sero-discordant couples, MSM, and young women at HIV risk,¹⁸⁻
260 ²⁰ which has been hypothesized to be a result of offering a strategy with demonstrated safety and
261 effectiveness and without a placebo. In those PrEP demonstration studies, HIV incidence has been very
262 low, and visits were generally quarterly and brief, suggesting that many who initiate PrEP in the context
263 of known safety and efficacy may not need intensive follow-up to achieve high adherence. In some high
264 income settings (e.g., San Francisco), delivery of PrEP at scale, layered onto high coverage of HIV testing
265 and ART delivery, has resulted in substantial reductions in new HIV infections in the past five years.²¹⁻²³

266 **HIV self-testing (HIVST) is an effective and recommended strategy to increase HIV testing**

267 In 2016, the WHO released a guideline which strongly recommended the implementation of HIVST as an
268 HIV testing strategy. HIVST was recommended to support the so called “first 90” of the Joint United
269 Nations Program on HIV/AIDS (UNAIDS) 90-90-90 targets (e.g., 90% of all people living with HIV will
270 know their status by 2020). HIVST has found to be appropriate at increasing HIV testing uptake and

271 frequency among diverse populations (e.g., key populations, sero-discordant couples, men, and women)
272 in a range of countries, including Kenya.²⁴ Additionally, HIVST may increase self-efficacy (e.g., knowing
273 one's HIV status), knowledge of partner's HIV status (one's personal risk), and awareness of one's PrEP
274 eligibility (when HIV-negative).

275 **Diverse models for PrEP referral + HIVST are needed**

276 In 2017, Kenya added PrEP to its national HIV prevention portfolio and began distributing free
277 government-issued PrEP to all individuals at HIV risk at select public clinics.^{13,14} While PrEP scale up in
278 Kenya has been relatively easy to implement among key populations (e.g., men who have sex with men
279 [MSM] and female sex workers [FSWs]) it has been difficult to scale up among AGYW at HIV risk. A study
280 conducted in Kenya among young women (16-20 years) which screened HIV risk and offered PrEP,
281 found that only 5% (9/168) eligible for PrEP initiated it.²⁵ Barriers to PrEP use among AGYW included
282 lack of PrEP knowledge, mistrust about PrEP efficacy and safety, low HIV risk perception, and
283 community-level barriers (e.g., stigma associated with PrEP use).²⁶

284 **In Kenya, young women have tight social networks that often influence health behavior**

285 Peer-delivered HIV prevention interventions have been found to be effective and feasible among key
286 populations with high social connectivity (e.g., MSM^{27,28} and FSWs^{29,30,31,32,33}). Similarly, young women
287 have tight peer networks and are often influenced by one another in terms of healthcare behavior. In a
288 HPTN-082 study conducted among AGYW in South Africa and Zimbabwe, 62% (254/409) of participants
289 reported being encouraged to uptake PrEP by peers.¹⁴ Similarly, in Kenya, informal peer PrEP referral
290 (e.g., word-of-mouth referral) was a major facilitator to PrEP uptake among AGYW.

291 **Peer PrEP referral + HIVST delivery is a novel approach that could reach AGYW at risk of HIV**

292 This pilot study and subsequent hybrid-randomized implementation trial for peer PrEP referral + HIVST
293 delivery will be the first model of its kind in sub-Saharan Africa. This approach is novel in its aim to build
294 upon existing informal (word-of-mouth) referral systems and its aim to function within existing peer
295 networks. This pilot study will be unique in its: 1) utilization of PrEP and HIVST- two innovations that have
296 been recently introduced by the Kenyan Ministry of Health (MoH), 2) training of PrEP users as "PrEP
297 champions", 3) implementation of HIVST to facilitate peer PrEP referral, and 4) implementation of a
298 hybrid-effectiveness randomization trial. The perceived acceptability and feasibility of this study are
299 supported by the formative stage of this research study (e.g., in-depth interviews and stakeholder
300 meetings) developed through a K99 grant.

301 **Findings from formative research on peer PrEP referral + HIVST**

302 As formative research for this project, in the first half of 2021, we conducted in-depth interviews with
303 AGYW using (n=15) and not using (n=15) PrEP to understand their perspectives and attitudes towards
304 HIV, HIVST, PrEP, and COVID-19. We additionally asked about their acceptability towards a peer PrEP
305 referral + HIVST delivery intervention. The median age of participants was 20 years (IQR: 20-22). Most
306 participants were in a relationship but unmarried (n=22; 73%) and nearly half (n=14; 47%) had one or
307 more children. 24 participants (80%) had tested for HIV within the last 3 months.

308 The main findings included that AGYW were often aware of HIVST although many had not used HIVST.
309 While some AGYW reported interest in HIVST for reasons including learning one's HIV status privately
310 and mitigating structural barriers associated with facility-based HIV testing (e.g., transportation costs,
311 long waiting times); other AGYW described reluctance accepting HIVST due to perceived lack of
312 knowledge and skills to perform the test accurately. Second, many AGYW were aware of PrEP although
313 rampant misinformation was evident. AGYW described that they (or their communities) often mistook
314 PrEP for post-exposure prophylaxis (PEP) or ARTs. Thereby stigmatizing PrEP use as it was associated

315 with persons engaging in risk behaviors or being HIV-positive. Third, we found that peer-delivered HIV
 316 prevention interventions may be of increased relevance following the COVID-19 pandemic as some
 317 AGYW reported changing partners during lockdowns while others described PrEP attrition during COVID-
 318 19 due to less frequent sexual activity and thereby lower perceived risk of HIV infection. Most importantly
 319 however, we found that most AGYW believed peer PrEP referral and HIVST delivery to be largely
 320 acceptable among Kenyan AGYW. Many participants expressed willingness to educate peers about
 321 PrEP use and side effects, to assist peers with HIVST and results interpretation, and to support peers
 322 with linkage to PrEP care and adherence. However, it should be noted that some participants mistrusted
 323 being approached by peers during a peer PrEP referral + HIVST model due to fear of involuntary HIV
 324 status or PrEP disclosure and its associated stigmatization. Example quotes highlighting findings above
 325 are presented in **Table 1**.

Table 1. Example quotes from AGYW during formative in-depth interviews

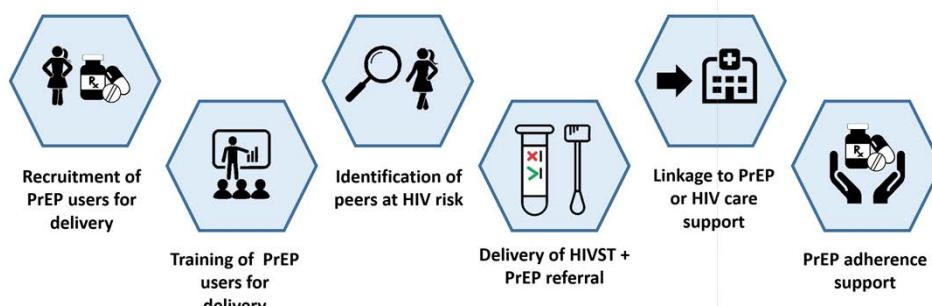
Perceptions about HIVST	<i>"I think (HIVST) it's good since you become aware of your (HIV) status. It's not a must you go to the hospital if you're afraid. If you have sex with someone and you fear going to the hospital, you need to test yourself" (PrEP user, age 21)</i>
Perceptions about PrEP	<i>"They (my peers) feel like they'll be stigmatized (for using PrEP), you know, mostly it is said that PrEP is majorly used by infected people. They haven't realized the difference between PrEP and HIV drugs" (PrEP user, age 20)</i>
Peer PrEP referral + HIVST model	<i>"I told them (peers) about PrEP...I tell them it doesn't have side effects, it is just like any other drug. When we meet, we just talk about it, I don't fear" (PrEP user, age 22)</i>

Findings from stakeholder meeting peer referral to PrEP + HIVST

326 On May 28, 2021 we convened a stakeholders' meeting with 34 participants from regulatory agencies
 327 and suppliers (e.g., Ministry of Health-, Pharmacy and Poisons Board, National AIDS & STI Control
 328 Programme, National AIDS Control Council), PrEP implementing partners (JHPIEGO, Clinton Health
 329 Access Initiative, Elton John AIDS Foundation), non-governmental organizations (e.g., LVCT Health, Bar
 330 Hostess Empowerment & Support Programme), health care providers (e.g., Kenyatta National Hospital,
 331 Ruiru Hospital), research institutions (e.g., Partners in Health & Research Development, Kenya Medical
 332 Research Institute, Jomo Kenyatta University of Agriculture and Technology), and young Kenyan women.
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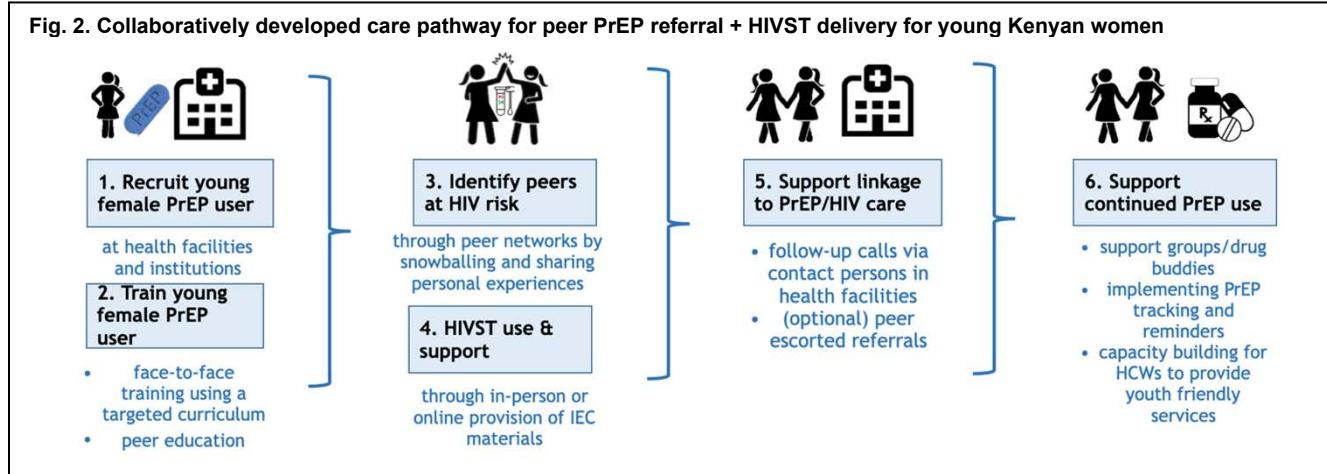
334 At this meeting, we first presented formative research findings on the acceptability and feasibility of the
 335 peer PrEP referral + HIVST delivery model among young Kenyan women to stakeholders. We then used
 336 the nominal group technique (NGT) to build consensus among stakeholders on the implementation
 337 strategies for the core components of this model to be including for pilot testing. The core components
 338 for which implementation strategies were developed included: 1) recruitment of PrEP users, 2) training
 339 of PrEP users for intervention delivery, 3) identification of peers at HIV risk, 4) delivery of HIVST and
 340 PrEP referral, 5) linkage to PrEP or HIV care support, and 6) PrEP adherence support (see **Fig. 1**). For
 341 the NGT, meeting participants first individually brainstormed implementation strategies for each core
 342 component that they then refined in small and large group discussions. Once the top implementation
 343 strategies for each component identified, individuals voted on the efficacy and feasibility of each strategy
 344 using 5-point Likert scale.

Fig. 1. Core components of the peer PrEP referral + HIVST delivery model for PrEP initiation among young Kenyan women



345 Overall, stakeholders were supportive of the peer PrEP referral + HIVST delivery model and felt that it
 346 would be acceptable and feasible among young Kenyan women. The highest scored strategies (by
 347 efficacy and feasibility ratings) were reviewed by stakeholders in the follow-up meeting (July 9th, 2021)
 348 and incorporated into care pathway for pilot testing, summarized in **Fig. 2**.

Fig. 2. Collaboratively developed care pathway for peer PrEP referral + HIVST delivery for young Kenyan women



349 **METHODS**

350
351 Taking PrEP to scale will require simplifying and diversifying models for delivery to achieve options that
352 are affordable, accessible, and meet the needs of AGYW and health systems. We have assembled a
353 multidisciplinary team to test peer PrEP referral + HIVST delivery. **We hypothesize that a formalized**
354 **peer referral model to PrEP will result in higher PrEP adoption (e.g., initiation and retention)**
355 **among AGYW compared to on-going informal referral models.**

356 **Study objectives**

357
358 1. To test and refine a peer PrEP referral + HIVST delivery model (Aim 1 pilot)
359 2. To determine adoption and feasibility of a peer PrEP referral + HIVST delivery model (Aim 1 pilot)
360 3. To identify weak points for peer a PrEP referral + HIVST delivery model (Aim 1 pilot)
361 4. To test a model of PrEP initiation through an implementation randomized trial and to analyze
362 study PrEP adoption, fidelity, cost, and safety (Aim 2 randomized trial)

363 *Hypothesis. AGYW will be interested in a model of peer PrEP referral + HIVST. Understanding the*
364 *potential weak points for peer PrEP referral will permit refinement of the intervention. Peer PrEP referral*
365 *+ HIVST will result in higher PrEP adoption (e.g., initiation and retention) compared to ongoing informal*
366 *referral models.*

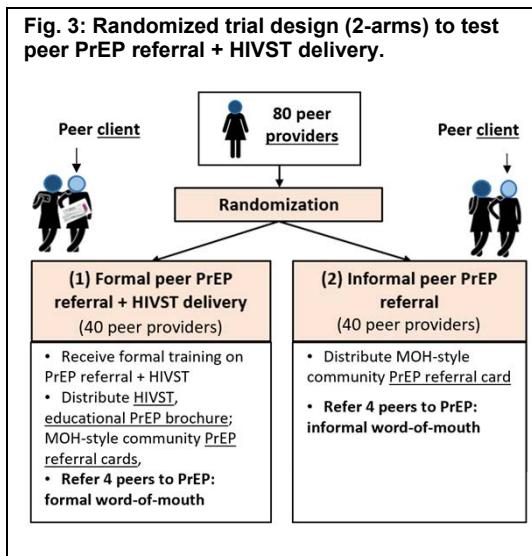
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368 **Research questions**

369
370 1. Will a peer PrEP referral + HIVST delivery model be adopted by and feasible among Kenyan
371 AGYW?
372
373 2. What are the weak points in a peer PrEP referral + HIVST delivery model for PrEP initiation?
374
375 3. How can these weak points be mitigated for a future peer PrEP referral + HIVST delivery
376 community-randomization trial?
377
378 4. How will a peer PrEP referral + HIVST delivery model compare in outcomes of PrEP adoption,
379 fidelity, cost, and safety compared to ongoing informal peer PrEP referrals (the current standard
380 of care)?

381 **Study design**

382 For Aim 1 (Objectives 1-3), we will conduct a one-arm
 383 intervention trial, or pilot study. There is no comparison arm in
 384 this pilot. The intervention we are testing was developed from
 385 extensive formative research, including analysis of data from
 386 in-depth qualitative interviews with young female PrEP users
 387 and non-users and a meeting with stakeholders.

388 For Aim 2 (Objective 4), we will subsequently conduct a two-
 389 arm hybrid type 3 randomized trial, in which young female
 390 PrEP users are randomized to: 1) “formal peer PrEP referral
 391 + HIVST delivery model” – where after training, participants
 392 are encouraged to refer 4 peers using PrEP educational
 393 materials and HIVST (2 HIVST kits/peer = 8 HIVST kits total)
 394 vs. 2) “informal peer PrEP referral”- where participants are
 395 encouraged to refer 4 peers to PrEP through word-of-mouth
 396 (**Fig. 3**).
 397

398 **Setting**

399 We will conduct the research for this study in Thika, Kenya (**Fig. 4**).
 400 Thika is an urban center, ~40 km outside of Nairobi in Central
 401 Kenya, which has a large peri-urban and rural surrounding
 402 population. HIV prevalence in Thika is 6%.³

403 We selected Thika, Kenya to conduct this research because the
 404 research team implementing the project here has extensive
 405 experience with the provision of PrEP to diverse populations. They
 406 were involved in the Partners PrEP Study clinical trial,⁸ then the
 407 open-label Partners Demonstration Project,³⁴ and are currently
 408 leading the Partners Scale-Up Project, MPYA study, POWER
 409 project, and pharmacy PrEP scale-up project. The site has technical
 410 expertise related to PrEP, community engagement with diverse
 411 populations (with high recruitment and retention >90%), and
 412 collaborative experience working with health providers outside of
 413 their own research clinics – precisely the components necessary for
 414 this work. The Thika research team also has extensive experience
 415 with the development of PrEP delivery models in Kenya – members
 416 of our study teams were deeply involved in the Kenya PrEP guideline process, including guidelines for
 417 clinical delivery.³⁵

419 **Aim 1: Pilot study procedures**

420 We have chosen a single-arm trial for the pilot study (i.e., no comparison to an informal peer PrEP referral
 421 arm) because this study is focused on testing the adoption and feasibility of a formal peer PrEP referral
 422 + HIVST delivery intervention and refining care pathways for this delivery model. Ongoing informal PrEP
 423 referral can still be observed and can serve as a general comparison in terms of demographics, PrEP
 424 uptake, and adherence.

425 **Participant eligibility & recruitment**

426 We will recruit 16 AGYW using PrEP for the pilot study. PrEP users will be identified from prior Partners

427 in Health and Research Development (PHRD) studies targeting AGYW and from public HIV clinics
 428 providing PrEP in Kiambu County. This will be a rolling recruitment and will end when all 16 participants
 429 have been identified. PrEP user participants will then be encouraged to refer 4 peers to PrEP, for a total
 430 of 64 peer study participants. The PrEP users will be trained on the importance of recruiting peers that
 431 are emancipated/mature minors only likely to benefit from using PrEP. This study sample size is deemed
 432 appropriate to measure the outcomes of interest and to refine the intervention care pathway prior to the
 433 randomized trial. This sample size is also similar in size to other PrEP implementation pilots led by the
 434 PHRD (**Table 2**). We will use the same recruitment strategies for both emancipated minors 16-17 years
 435 and women ≥ 18 years.³⁶

436

Table 2. Eligibility and recruitment strategies- pilot study			
	Eligibility	Ineligibility	Recruitment Strategies
PrEP users (n=16)	<ul style="list-style-type: none"> • >16- to 24 years old³⁶ • Female • Adherent to PrEP (i.e., self-report taking PrEP all the time) • Can identify 4 peers at HIV risk who would be interested in PrEP • Able & willing to provide written informed consent 	<ul style="list-style-type: none"> • < 16 years old, > 24 years old • Male • Not adherent to PrEP • Cannot identify 4 peers who would be at HIV risk and/or interested in PrEP • Is not able or willing to provide written informed consent 	<ul style="list-style-type: none"> • Recruit participants from prior AGYW studies • Recruit participants from HIV clinics where PrEP is available using PHRD recruitment strategies (e.g., workshops for HCWs) • Strategies developed from the formative research and stakeholder meetings
Peers (n=64)	<ul style="list-style-type: none"> • Age ≥ 16 to 24 years* • Female • Referred by peer (i.e., a PrEP users) to initiate PrEP • Able & willing to provide informed consent 	<ul style="list-style-type: none"> • Age < 16 or > 24 years • Male • Not referred by peer (i.e., a PrEP users) to initiate PrEP • Not able and willing to provide informed consent 	<ul style="list-style-type: none"> • Peer referral from PrEP users

437

Pilot procedures

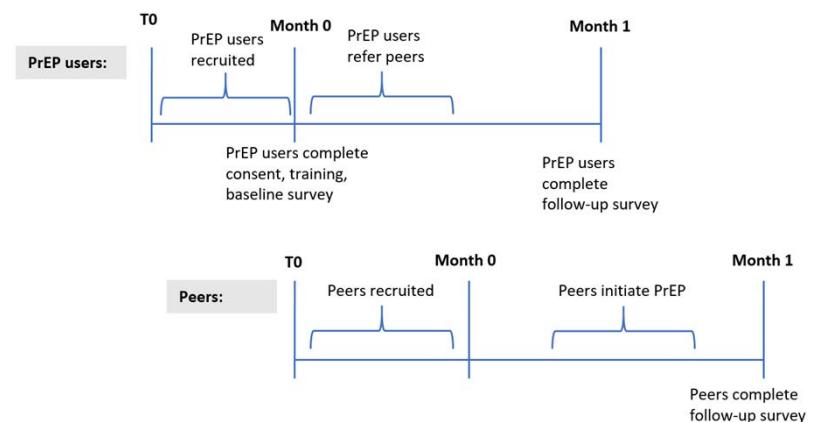
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439 All participants will be enrolled in the
 440 pilot study and followed for 1 month,
 441 as outlined in **Fig. 5**.

442

PrEP users. Once all PrEP users
 443 have been recruited and identified,
 444 they will complete a 1-day in-person
 445 group training (with appropriate
 446 COVID precautions in place) on the
 447 peer PrEP referral + delivery model
 448 (Month 0). This training will include
 449 education on HIV risk screening, HIV
 450 prevention, HIVST use (including
 451 results interpretation), PrEP
 452 adherence and safety, and the
 453 importance of confidentiality. With reference to the Rapid Assessment Screening Tool for PrEP (RAST),
 454 PrEP users will be taken through the eligibility criteria or risk factors that would warrant individual peers
 455 qualify to be initiated on PrEP. All PrEP users will be given educational resources on PrEP and HIVST
 456 (approved by the trial IRB) that they can share with their peers, including a list of locations in Thika where
 457 PrEP is provided for free (by Kenyan Ministry of Health [MoH]). Additionally, all PrEP users will receive 8
 458 HIVST kits and be encouraged to use these (2 HIVST kits per peer) to refer 4 peers to PrEP. We will
 459 complete all enrollment procedures with PrEP users at the beginning of the group training, and all PrEP
 460 users will complete the quantitative baseline survey before training and complete a short post-training

Fig. 5. Timeline of pilot enrollment and follow-up



461 questionnaire to assess understanding of key components of HIVST and PrEP at the end of the group
462 training. We will follow-up with all PrEP users in-person or remotely 1 month following this training to
463 complete a structured questionnaire and collect self-reported outcomes, including the number of peers
464 referred and PrEP initiation among peers (see Data analysis & outcomes section). During the COVID-19
465 pandemic, the Kenyan research team has successfully completed a number of remote questionnaires
466 and in-depth interviews for other PrEP implementation and COVID-19 studies.

467

468 Peers. PrEP users will refer peers to the study using a recruitment script given to them at the training.
469 The peers that are interested in HIVST, PrEP for HIV prevention, and study participation will call study
470 staff (study team number specified in the recruitment script) before receiving the intervention from PrEP
471 users so the study team has their contact information and can reach them 1 month later to complete a
472 follow-up questionnaire. PrEP users will then deliver PrEP promotional materials and HIV self-tests to
473 interested peers. The information of study staff and locations where peers can go to access free PrEP
474 and HIV treatment services will be included in the promotional materials so peers can contact the study
475 staff if they have any questions about PrEP, HIVST, or linkage to care. For peer follow up, research
476 assistants will call peers 1 month following when they received the intervention from PrEP users (and
477 gave their contact information to study staff) to complete a formal consent process and a structured
478 quantitative questionnaire either remotely or in-person (at the research site or at their home).

479

480 All participants will receive transportation reimbursement and an additional 300 KES (~\$2.70 USD) to
481 compensate for their time and effort and for completion of a structured questionnaire at baseline (PrEP
482 users) or follow-up (PrEP users and peers). PrEP users will also receive an additional small incentive for
483 participation in training and peer recruitment activities. For participants that have to complete
484 questionnaires remotely, we will send mobile money to reimburse participants.

485 *Intervention core components*

486 Throughout the duration of the study, participants will support the implementation of the peer PrEP
487 referral + HIVST model through core components identified in the stakeholder meetings (**Fig. 1**).

488 1. Recruit young female PrEP users – through health facilities and institutions. Specifically, study
489 counsellors and healthcare workers (HCWs) will identify young women who can serve as “PrEP
490 champions” (i.e., display knowledge about PrEP, engage in PrEP adherence, and have the ability to
491 recruit/train peers).

492 2. Train young female PrEP users – through a 1-day in-person group or individualized training using
493 a targeted curriculum. It is vital that training is appropriate to the AGYW age group (e.g., information
494 is comprehensible, engaging). Further, this approach may be combined with elements of peer
495 education, an approach which had similar ratings in terms of effectiveness and feasibility. Peer
496 education is deemed appropriate to educate AGYW in terms of HIVST use and interpretation as well
497 as PrEP use, efficacy, and side effects.

498 3. Identify peers at HIV risk – through peer networks. Participants will identify peers through
499 snowballing methods and will approach the topic of PrEP by demonstrating emotional support to peers
500 (e.g., sharing personal experiences using PrEP).

501 4. HIVST use and support – through the in-person or online provision of information, education, and
502 communication (IEC) materials. These materials may include posters, graphics, package inserts
503 (HIVST kits) or pamphlets to aid researchers and healthcare workers teaching AGYW about HIVST
504 and PrEP.

505 5. Support linkage to PrEP or HIV care – through information provided in the PrEP pamphlet shared

506 with them by PrEP users, which includes the contact information of study staff that can help support
507 linkage to care and the information for nearby health facilities that provide free PrEP services.
508 Additionally, PrEP users will be trained on how to guide peers on linkage to nearby free PrEP services
509 and may escort peers to these services if peers request this and they feel comfortable doing so. PrEP
510 users who support their peers via escorted referrals will be asked to encourage peers to return for
511 PrEP refills without escorted referrals to mitigate peer dependency.

512 6. Support continued PrEP use – through the implementation of peer support groups and drug-
513 buddies. Drug-buddies refer to peers who are paired and can hold one another accountable to daily
514 PrEP use. PrEP adherence will also be combined with a formalized PrEP reminder and tracking
515 system (e.g., USHAURI phone application). Further, continued PrEP use will be supported through
516 the implementation of capacity building activities among healthcare workers to provide youth friendly
517 PrEP services.

518 The PrEP medication will be provided for free from the public health clinics via the Kenyan MoH and HIV
519 self-tests for this pilot study will be provided for free via ChemBio Diagnostics Systems.

520 This pilot study will be conducted during the ongoing COVID-19 pandemic. As such, the pilot study will
521 be conducted in accordance with the Kenyan COVID-19 prevention measures in place at the time of the
522 study. Participants will be asked/screened about symptoms of COVID-19 (including temperature) prior to
523 entering the PHRD study site for a follow-up appointment, all in-person data collection will be conducted
524 with appropriate distance, ventilation, and participants will be asked to wear a face mask to reduce the
525 risk of COVID-19 infection. As necessary, we will explore options to complete surveys over the phone.

526 Condoms will be available through the PHRD research site but are not included in the package of PrEP
527 services provided in this study.

528 *PrEP medication*

529 Tenofovir disoproxil fumarate (or TDF, 9-[(R)-2-[[bis [[(isopropoxycarbonyl) oxy] methoxy] phosphinyl]
530 methoxy] propyl] adenine fumarate), emtricitabine (or FTC, 5-fluoro-1-(2R,5S)-[2-(hydroxymethyl)-1,3-
531 oxatholan-5-yl]cytosine), and lamivudine (or 3TC, 2',3'-dideoxy-3'-thiacytidine 4-Amino- 1-[(2R,5S)- 2-
532 (hydroxymethyl)- 1,3-oxathiolan-5-yl]- 1,2-dihydropyrimidin- 2-one) are reverse transcriptase inhibitors
533 that have been approved for the treatment of HIV infection in humans in Kenya and the United States.
534 A fixed-dose, oral co-formulation of FTC/TDF (Truvada®) has also been approved for HIV prevention
535 in Kenya and the United States. The WHO recommends TDF-containing medications as PrEP, which
536 includes TDF combined with FTC as well as potentially TDF alone and TDF combined with lamivudine
537 (or 3TC, a medication closely related to FTC). Any TDF-containing medications that align with WHO
538 and Kenyan national guidelines for PrEP will be used in this study. PrEP will be prescribed for once-daily
539 oral use. Study medication will be provided by the Kenyan MoH and stored in accordance with the drug
540 manufacturer's recommendations.

541

542 *PrEP discontinuation*

543 PrEP initiation and continuation will be in accordance with the Kenyan PrEP guidelines. Use of PrEP
544 may be interrupted by the site investigators or Kenyan clinicians due to safety concerns for the participant
545 or use of concomitant medications that could interfere with PrEP or present a safety concern. All
546 treatment interruptions will be documented.

547

548 *Referral to continued PrEP care*

549 For participants that wish to continue PrEP use following the pilot study (1-month trial duration);

550 participants will remain enrolled in PrEP at the healthcare facility at which they had enrolled/initiated in
 551 PrEP use. PrEP will then be prescribed and administered via this physician who will provide 3-month
 552 supplies of PrEP.

553 *HIV Self-Testing Kit*

554 ChemBio (who has committed to providing HIVST kits to the
 555 pilot study) manufactures the SURE CHECK® HIV 1/2 Assay
 556 (**Fig. 6**), a blood-based HIVST that has 99.7% sensitivity,
 557 99.9% specificity, presents results in 15 minutes, and is
 558 approved by the US FDA.³⁷ Results are easy to read (1 line:
 559 HIV-negative, 2 lines: HIV-positive, no lines: invalid result).
 560 HIVST serves as a preliminary test result and must be
 561 followed-up with confirmatory facility-based HIV testing to
 562 indicate a diagnosis.

Fig. 6. Sure Check HIV 1 / 2 assay



563 *Data Collection*

564 Quantitative data will be collected through surveys at baseline (Month 0) and follow-up (Month 1) and
 565 focus group discussions (FGDs) will be completed near the end of the pilot (Month 3).

566 Quantitative surveys. Trained research assistants (RAs) stationed at healthcare facilities delivering PrEP
 567 will approach eligible individuals and invite them to
 568 participate in the study. They will review the informed
 569 consent form with these individuals and answer any
 570 questions they may have regarding participation. Once
 571 written informed consent is obtained, RAs will conduct a
 572 structured quantitative survey with the participant. **Table**
 573 **3**. outlines the data collection activities which will be
 574 conducted among the participant (PrEP user) and the
 575 recruited peers at baseline (Month 0) and follow-up (Month
 576 1). All quantitative data will be collected on a tablet using
 577 CommCare (Dimagi, Cambridge, USA), an electronic data
 578 collection platform.

Table 3. Data collection activities

Variables	PrEP user M0	M1	Peer M1
Demographics	X		X
HIV risk	X		X
Depression ^{38,39}	X		X
Sexual health/HPV	X		X
Self-efficacy ⁴⁰	X		X
Peer support	X		X
HIVST distribute/use		X	X
PrEP initiation/use	X	X	X
PrEP/HIV stigma	X	X	X

579 FGDs. We will conduct FGDs with about 12 PrEP users who delivered and about 12 peers who received
 580 the peer PrEP referral + HIVST delivery model. We will conduct 4-5 FGDs in total (3-6 participant/FGD);
 581 of these 2-3 FGDs will be conducted among PrEP users (recruiters) and 2-3 FGDs will be conducted
 582 among peers (those recruited to the study). We hereby aim to explore their experiences with this new
 583 PrEP delivery model and understand the acceptability of a peer PrEP referral + HIVST model. FGDs will
 584 utilize the Consolidated Framework for Implementation Research (CFIR)⁴¹ to understand model
 585 acceptability, measure model weak points (barriers) and to assess model facilitators in order to inform
 586 the subsequent randomization trial. Topics discussed in the FGDs are summarized in **Table 4**. All
 587 participants that participate in these focus group
 588 discussions will sign documents of informed consent.
 589 Additionally, all participants will be reimbursed for
 590 transportation and an additional 300 KES (~\$2.70 USD)
 591 for participation in FGDs.

592 All qualitative FGDs will be conducted in the participant's
 593 preferred language (English or Kiswahili) by trained

Table 4. FGD themes, informed by CFIR domains: constructs

Intervention: complexity	Clarity of instructions/logistics
Outer: peer pressure	Peer influence on HIVST use, PrEP initiation
Individual: self-efficacy	Confidence to initiate PrEP, use HIVST
Individual: knowledge	Understanding of PrEP benefits, HIV risk
Process: Executing	Experiences delivering model/materials
Process: Reflecting	Attitudes towards the model, identify weak points

594 qualitative research assistants using pre-piloted, semi-structured interview guides. Each FGD will be
 595 audio recorded, transcribed, and translated into English by study team members who will also routinely
 596 complete debriefing reports⁴² to accelerate real time learning. Dr. Ngure, an experienced behavioral
 597 scientist who has led our qualitative research in Thika for the past decade, will supervise these
 598 discussions.

599 *Data analysis & outcomes*

600
 601 Quantitative surveys. **Table 5** shows the study outcomes that will be obtained from the quantitative
 602 surveys. For Aim 1 (Objective 1), we will calculate the number and proportion of participants who initiated
 603 PrEP at healthcare facilities, peers referred to PrEP, and peers that used HIVST. These outcomes will
 604 be measured along outcomes of “acceptability,” “appropriateness,” and “feasibility” (Objective 2).

Table 5. Outcomes for the peer PrEP referral + HIVST delivery pilot and measured at Month 1. * primary		Metric of success: Allow seamless progression to trial	
Outcome:	Details:	Reported:	
PrEP initiation*	Prop. of referred peers that initiated PrEP*	Peers and PrEP users	40% of those followed up (n≥19)
PrEP referral	No. of peers referred to PrEP	PrEP users	≥3 peers per PrEP user (n≥48)
HIVST use	Prop. of referred peers that used HIVST	Peers	75% of those followed up (n≥36)

605
 606 FGDs. Transcripts will be reviewed separately by two or more qualitative researchers, who will ensure
 607 completeness. These researchers will immerse themselves in the data through repeated readings of the
 608 transcripts and create a preliminary codebook of inductive^{43,44} and deductive^{45–47} codes to capture the
 609 experiences of AGYW regarding a peer PrEP referral + HIVST model including barriers and facilitators
 610 (Objective 3). A sample of transcripts will be double coded independently by two or more researchers,
 611 with coding discrepancies identified and resolved via consensus. During this process, the codebook will
 612 be refined, with existing codes combined, separated, or eliminated and new codes added as needed to
 613 capture emerging themes.^{48,49} Thereafter, remaining transcripts will be coded in Dedoose (Los Angeles,
 614 California, USA) or Nvivo 12 (QSR International, Melbourne, Australia). We have extensive experience
 615 analyzing qualitative data to inform intervention development.^{50–72}

616 *Participant retention and withdrawal*

617 The Thika research site will develop retention methods tailored to and most efficient for the local study
 618 settings. Retention activities may include explanation of the study schedule (i.e., return for follow-up after
 619 one month) and procedural requirements during the informed consent process. Further, peers referred
 620 to the study, will be contacted and directed to the PHRD study site for follow-up or will be visited (e.g., at
 621 home) by PHRD researchers. However, should the aimed sample size not be attained (e.g., < 75%
 622 referral rate), then alternative follow-up strategies may be implemented including 1) giving peers mobile
 623 money conditional on texting researchers their contact information or 2) having PrEP users report
 624 outcomes for their peers.

625 Participants may voluntarily withdraw from the study for any reason at any time. The site investigators
 626 may also withdraw participants from the study in order to protect their safety and/or if they are unwilling
 627 or unable to comply with required study procedures. Reasons for withdrawal will be recorded.

628 *Limitations*

629
 630 This pilot study has some potential limitations that are important to note. First, some of the participants
 631 may be recruited for this study from prior or ongoing PHRD studies targeting AGYW. These participants
 632 may not accurately represent PrEP and HIVST knowledge among AGYW who have not been enrolled in
 633 prior PrEP and HIVST interventions. We aim to mitigate this challenge by recruiting other participants

634 from public HIV clinics who have no prior PrEP and/or HIVST education.

635
636 Additionally, the pilot study will encourage participants to recruit 4 peers to the study. The limitation of 4
637 peers may inherently exclude some AGYW who maintain at high risk of HIV and would be interested in
638 PrEP initiation through a peer PrEP referral+ HIVST model. Further, those recruited to the pilot study will
639 be provided 2 HIVST kits to test themselves (independently or with the assistance from the PrEP user)
640 or to test a primary sexual partner. Some AGYW may benefit from testing multiple sex partners (e.g., in
641 sex worker relationships). Although a focus on partner testing is outside the scope of this study- future
642 research should be considered in this area.

643
644 Finally, in the pilot study, peers recruited to the study are supplied HIVST kits free of cost (from ChemBio).
645 In settings outside of a research or intervention setting, AGYW may have to purchase HIVST kits at cost
646 which may influence the appropriateness and feasibility of this model. The randomization trial will further
647 research this factor through a cost analysis.

648 649 **Aim 2: Randomization trial procedures**

650 651 *Study population*

652 Based on confusion with naming conventions from the pilot study, we have revised our description of
653 PrEP users and peers to the following: “peer providers” and “peer clients.” From here on out, peer
654 providers (formerly “PrEP users”) will be young women using PrEP who will receive training on the peer PrEP
655 referral + HIVST delivery in the intervention arm or who will continue with informal models of peer PrEP
656 referral in the standard-of-care control arm. Peer clients (formerly “peers”) will then be the young women
657 that receive the peer PrEP referral + HIVST intervention delivered by the peer providers. For reporting
658 purposes, we will also refer to peer providers as “index peers” and peer clients as “referred peers.”

659 We will recruit 80 young female peer providers from public healthcare clinics delivering PrEP in Kiambu
660 County and neighboring Counties using established PHRD site techniques. These participants will further
661 refer 4 peer clients each to PrEP for a maximum 320 potential peer clients.

662 Eligibility criteria.

663

664 **Peer providers.** Eligible peer providers will be: i) female, ii) ≥ 16 to 24 years old (including emancipated
665 minors ≥ 16 to 17 years³⁶), iii) must have refilled or initiated PrEP (i.e., been dispensed PrEP), iv) are able
666 to identify 4 peers at risk of HIV infection who may be interested in PrEP, v) not currently enrolled in
667 another HIV study, and vi) are able and willing to be randomized to the intervention, complete research
668 activities, and provide written consent (**Table 6**). Due to the nature of the training intervention which
669 includes slides, quizzes, and other activities that involve reading and writing, peer providers will be
670 considered ineligible if they do not have basic literacy skills. Due to some challenges recruiting young
671 female peer providers in the Aim 1 pilot, we made some modifications to the inclusion criteria in this
672 section, including reducing the duration of PrEP use and dropping the requirement for PrEP disclosure.

673

674 **Peer clients.** Eligible peer clients will be: i) female, ii) ≥ 16 to 24 years old (including emancipated minors
675 ≥ 16 to 17 years³⁶), iii) referred by a peer provider to initiate PrEP, and iv) are able and willing to provide
676 informed consent.

677

678 **Recruitment strategies.** **Peer providers.** Peer providers will be recruited through a multipronged approach
679 that will include recruitment through other ongoing PrEP research projects, and from nearby public health
680 facilities implementing PrEP programs, such as, workshops for healthcare workers, use of IEC materials,
681 and working with community health workers to identify potential participants. Peer providers will be

682 compensated 300 KES (~\$2.70 USD) and be reimbursed for travel at their baseline appointment and
683 again at their 3-month follow-up appointment. No travel reimbursement at follow-up will be provided if
684 follow-up questionnaires are conducted via phone. All peer providers will be encouraged to disclose PrEP
685 use to peers, although this is not required. Study counselors will conduct follow-up calls with peer
686 providers to check in and see how the referral process is going and answer any questions or concerns
687 regarding the intervention. Recruitment of peer providers will be on a rolling basis, so it is possible that
688 peer providers and peer clients may not be mutually exclusive (as future peer providers could be previous
689 peer clients).

690 *Peer clients.* Peer providers will recruit peer clients. Peer clients will contact study counselors (via phone),
691 to provide RAs with contact information to schedule a follow-up visit (Month 3) at the PHRD study site
692 (transport refunded) or via phone interview. Clients won't be engaged in study activities at Month 3 until
693 they have provided informed consent. To help prompt peer providers to remind peer clients to call
694 research staff at the point of recruitment (a challenge during the pilot study), we will compensate peer
695 providers and their peer clients a small amount (150 KES each, ~\$1.40 USD each) each time a peer
696 client pings the study phone line to enroll in the study. For any peer clients who do not ping the study
697 phone, study staff will attempt to collect contact information for the peer clients from the peer providers
698 during a follow-up visit/call. The peer client can still decline enrollment when contacted by study staff.
699 Peer clients will be compensated 300 KES (~\$2.70 USD) and reimbursed for travel for attending the 3-
700 month follow-up appointment. No travel reimbursement will be provided if the questionnaires are
701 conducted over the phone. To facilitate the delivery of this compensation, we will use a secure mobile
702 money platform (M-Pesa) that we have used successfully for other research projects. Research staff will
703 call these individuals twice (one week apart) and stop trying to contact these potential participants if these
704 phone calls do not go through. Additionally, they will do their best to confirm the identity of the potential
705 peer client before describing any details of the research study (and their potential participation in this
706 study).

707

708 Consenting procedures. *Peer providers.* All peer providers that meet eligibility requirements will provide
709 written informed consent at the point of recruitment and prior to randomization with a trained research
710 assistant. This signed consent form will be stored as confirmation of informed consent and a copy will be
711 made available to the participant.

712 *Peer clients.* All peer clients that have contacted the study team directly, expressed interest in the study,
713 and have met eligibility requirements will complete informed consent at the Month 3 follow-up visit, before
714 completing any questionnaires assessing their experience with the peer PrEP referral + HIVST
715 intervention or informal peer PrEP referral process. Those unable or unwilling to come to the PHRD site
716 to sign a consent form will have the option to provide verbal consent over the phone. If verbal consent
717 was provided, the trained research assistant will note the date that verbal consent was obtained on a
718 copy of the consent script. The signed consent form and scripts will be stored as confirmation of informed
719 consent. A subset of peer clients who sign the written consent form will also be asked to provide a DBS
720 sample collected from a finger prick or venous blood. No peer client providing verbal consent will be
721 asked to provide a DBS sample.

722

723

Table 6. Eligibility and recruitment strategies- randomized trial

	Eligibility	Ineligibility	Recruitment Strategies
Peer providers (formerly “PrEP users”) (n=80)	<ul style="list-style-type: none"> • ≥ 16- 24 years old³⁶ • Female • Must have refilled or initiated PrEP (i.e., been dispensed PrEP) • Not currently enrolled in an HIV study • Can identify 4 peers at HIV risk who could benefit from PrEP • Able & willing to be randomized to the intervention, participate in research activities, and/or provide written informed consent 	<ul style="list-style-type: none"> • Not between 16-24 years old • Male • Have not used PrEP • Cannot identify 4 peers who would benefit from PrEP • Is not able or willing to be randomized to the intervention, participate in research activities, and/or provide written informed consent • Currently enrolled in an HIV study • Illiterate 	<ul style="list-style-type: none"> • Recruit participants from HIV clinics where PrEP is available using PHRD recruitment strategies (e.g., workshops for healthcare workers) • Strategies developed and refined during the pilot study
Peer clients (formerly “peers”) (n=320)	<ul style="list-style-type: none"> • Age ≥ 16 to 24 years • Female • Referred by peer provider (i.e., a “PrEP user”) to initiate PrEP • Able & willing to provide informed consent 	<ul style="list-style-type: none"> • Age < 16 or > 24 years • Male • Not referred by peer provider (i.e., a PrEP users) to initiate PrEP • Not able and willing to provide informed consent 	<ul style="list-style-type: none"> • Peer providers will recruit peer clients. At point of recruitment, peer clients will call research staff to provide contact info for follow-up • At follow-up, peer providers share the contact information of peer clients so they can be reached for follow-up. • If peer client calls the study staff, both the peer client and provider will be compensated 150 KES via mobile money.

724

725

Randomization

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Shortly after trial enrollment, peer providers will open in the presence of a study RA an opaque sealed envelope sequentially distributed to them that has their randomization arm specified inside (e.g., formal peer PrEP referral + HIVST arm; informal peer PrEP referral arm).

Study procedures & intervention

731

732

Depending on the arm peer providers are randomized to, the following procedures will apply (**Table 7, and Figure 7**):

Table 7. Interventions/materials received by peer providers and peer clients in the intervention and control arms

Intervention/material	Intervention arm		Control arm	
	<i>Peer provider</i>	<i>Peer client</i>	<i>Peer provider</i>	<i>Peer client</i>
Formal 1-day training on PrEP & HVIST	X			
Formalized conversation about PrEP, HIVST & referral	X	X		
PrEP educational brochure	X	X		
HIVST kits for distribution/self-testing	X	X		
WhatsApp group for questions	X			
PrEP referral card	X	X	X	X
Informal conversation about PrEP & referral			X	X

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[Intervention arm]: Formal peer PrEP referral + HIVST delivery (n=40 peer providers). Peer providers randomized to this intervention arm will receive a training on PrEP referral and HIVST delivery. We will train peer providers in groups of around 4-8 peer providers. The training materials will be based on Kenya’s national PrEP guidelines and delivered in a 1-day session led by experienced research staff. The training will cover HIV prevention methods, how to use and interpret HIVST kits, how to initiate conversation with peers about PrEP, practice scenarios, pre-training and post-training quizzes, and other related activities. Based on feedback from the Objective 2 FGDs, we modified the pilot training materials

740 to also include more training on HIVST interpretation, common PrEP misconceptions, issues surrounding
741 PrEP stigma, reminders for consistent PrEP use, and the importance of delivering the intervention
742 package to peers privately.

743 Following the training, peer providers will be asked to identify 4 peer clients they perceive as at HIV risk
744 and think might be interested in daily oral PrEP and deliver the intervention to these individuals. This
745 intervention arm will include a formalized conversation about PrEP with peers, delivery of HIVST kits,
746 sharing a PrEP & HIVST educational brochure, delivery of a PrEP referral card, and access to a
747 (monitored) WhatsApp group to ask questions and for support (**Table 7 and Figure 7**):

- 748 • **Formalized PrEP conversation.** Peer provider in this intervention arm will be trained on techniques
749 they can use to start conversations with their peer clients about PrEP and provide correct information
750 about PrEP effectiveness, use, and safety (and answer any questions related to these). Additionally,
751 they will deliver a study-developed PrEP and HIVST informational brochure to peer clients that covers
752 the talking points about PrEP use and safety and can be used by as a reference in the future.
- 753 • **HIVST kit delivery.** The intervention will include the distribution of 2 HIVST kits by peer providers to
754 each peer client. With delivery of the HIVST kits, peer providers will be trained to share information
755 on how to use the HIVST kits with peer clients and direct them to the information and pictorial brochure
756 that comes with the HIVST kits for more information as needed. Referred peer clients can use the
757 HIVST kits to test themselves for HIV, test for HIV with a peer, or test a main sexual partner (if they
758 feel comfortable) which may increase feelings of self-efficacy and knowledge of PrEP eligibility or
759 need – potentially facilitating PrEP initiation.
- 760 • **PrEP educational brochure:** This informational brochure will reinforce key points of the training
761 session provided to peer providers. It will be delivered by peer providers to peer clients during the
762 formalized PrEP conversation.
- 763 • **PrEP referral card.** The intervention will also include the delivery of a PrEP referral card by peer
764 provider to peer clients with training on how to help peers link to PrEP services if needed. On this
765 card will be listed information on the location of nearby public clinics and in neighboring counties with
766 free PrEP services and that peer client can ask for when they arrive for assistance with PrEP services.
767 This referral card will also contain the study phone number to support peer clients that wish to go to
768 another facility for PrEP support.
- 769 • **WhatsApp Group.** The study team will answer questions, provide additional information, and promote
770 discussion between peer providers through a monitored WhatsApp group (participation is optional).
771 This forum has been used in other studies at PHRD and we plan to implement several measures to
772 make these groups as confidential as possible. First, individual WhatsApp groups will be created for
773 each peer provider training session. That way, peer providers that participate in this option will only
774 be conversing with individuals they met during their training session. Second, during the training
775 session, peer providers will be instructed to not disclose any identifying information about peer clients
776 in the WhatsApp group. Third, a study team member will be assigned to monitor the group 24/7. If
777 necessary, study staff will delete any messages that contain personal information about participants
778 immediately. The study staff monitoring the group will also periodically delete older messages, so
779 they are not stored long-term. Finally, the WhatsApp groups will only be available during the 3 month
780 intervention time period and then all remaining messages from that group will be permanently deleted.
- 781
- 782
- 783

784 Peer providers randomized to this arm will be encouraged to disclose PrEP use to peers, although this
785 is not required.

786 [Control arm]: Informal peer PrEP referral (n=40 peer providers). Peer providers randomized to this

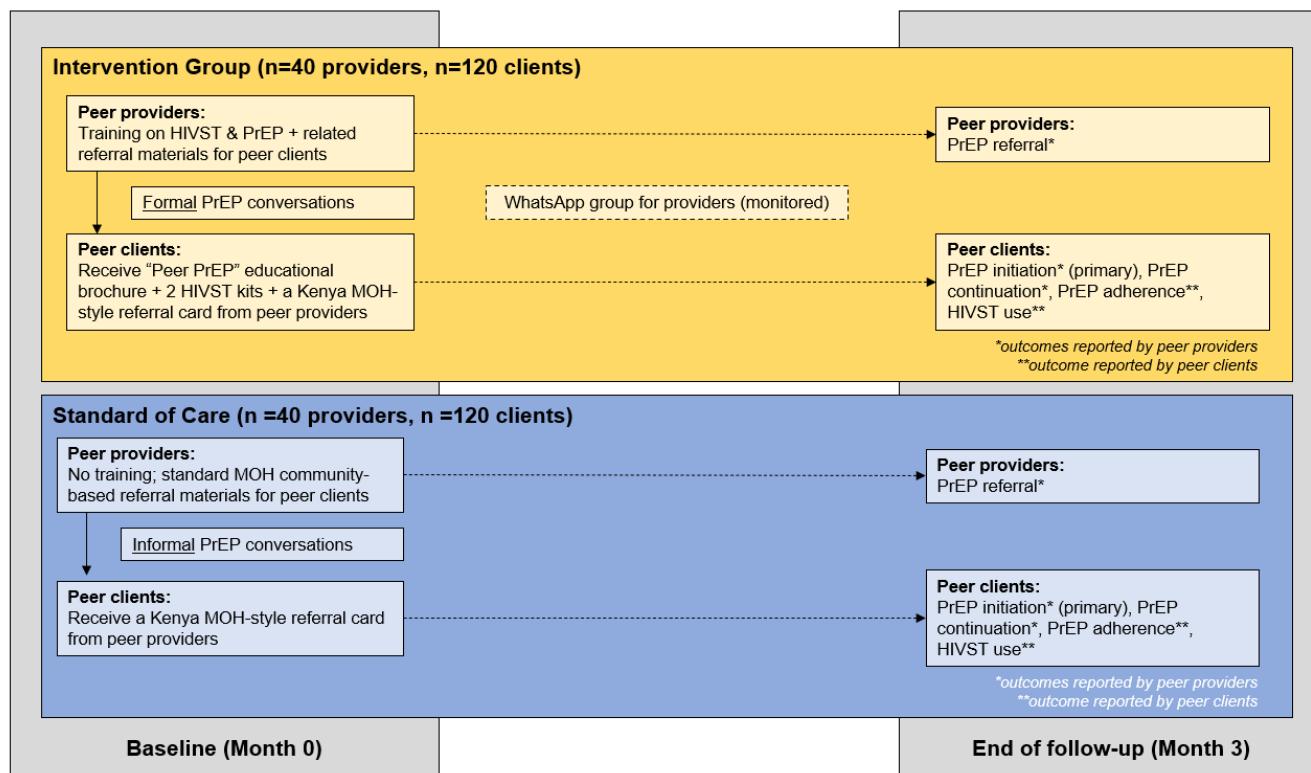
787 control arm will be encouraged to refer 4 peers that they perceive to be at HIV risk and would be interested
 788 in daily oral PrEP through free public PrEP services. This control arm will include informal conversations
 789 about PrEP with peers (as per the standard of care) and delivery of a PrEP referral card (**Table 7 and**
 790 **Figure 7**):

- 791 • **Informal PrEP conversations.** Peer providers in this arm will not receive any formalized training on
 792 PrEP or HIVST and will not receive any HIVST kits for distribution to peers. They will be encouraged
 793 to talk with their peers about PrEP in the way that feels most comfortable to them and in way they
 794 would typically have conversations about new products (e.g., lipstick) or things that interest them.
- 795 • **PrEP referral card.** This control arm will also include the delivery of a PrEP referral card by peer
 796 providers to peer clients. This will be the same referral card as that delivered to peer clients in the
 797 intervention arm, with information of nearby public clinics with free PrEP services. This referral card
 798 will also contain the study phone number so peer clients remember to ping the study counselor when
 799 these informal conversations occur and to support peer clients that wish to go to another facility for
 800 PrEP support.

801 Like in the intervention arm, peer providers randomized to this arm will be encouraged to disclose PrEP
 802 use to peers, although this is not required. No WhatsApp group will be available in this arm.

803

804 **Fig. 7. Study procedures for intervention, and standard of care groups.**

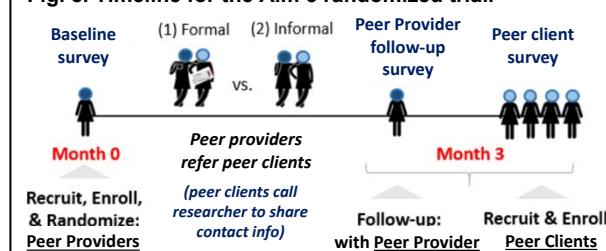


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809 **Data Collection**

811 **Overview.** **Fig. 8** highlights a timeline of study visits and
 812 data collection activities for this trial. There are two data
 813 collection time points in this study: Month 0 (peer
 814 provider baseline questionnaire) and at Month 3 (peer
 815 provider follow-up questionnaire and peer client follow-
 816 up questionnaire). After providing informed consent, all
 817 peer providers enrolled in the trial will complete a
 818 baseline (Month 0) and follow-up (Month 3) survey.
 819 Additionally, all peer clients who voluntarily provide their
 820 contact information directly to the study team and request to be enrolled in the study will be contacted to
 821 schedule an interview at Month 3. The peer client will be screened for eligibility and consented prior to
 822 completing a follow-up survey at Month 3. This timeline will provide recruited peer clients with the
 823 opportunity to enroll in PrEP (approx. 1 month following the baseline survey) and return to healthcare
 824 facilities for one PrEP refill (approx. 3 months following the baseline survey). Sociodemographic
 825 information will be collected at baseline among peer providers and follow-up among peer clients (i.e.,
 826 their first research visit). At all follow-up visits, we will measure both self-reported outcomes related to
 827 adoption of PrEP services, as well as process-level outcomes (e.g., number of HIVST kits received in the
 828 intervention arm, PrEP referral cards received in both arms), and implementation outcomes (e.g.,
 829 intervention acceptability, appropriateness, fidelity, satisfaction).

Fig. 8. Timeline for the Aim 3 randomized trial.

831 **Setting.** Experienced quantitative researchers will collect electronic data using CommCare (Dimagi,
 832 Cambridge, USA), an electronic data collection tool, in questionnaires at baseline (Month 0) and follow-
 833 up (Month 3). While we will encourage all enrolled peer clients to come to the PHRD research site to
 834 complete the questionnaires in person, we will additionally allow for the option of questionnaire
 835 participation/completion over the phone to allow for easier engagement in follow-up activities (in
 836 particular, peer clients that might have been recruited outside of Kiambu County). Peer providers will
 837 need to come in-person to the clinic during baseline to receive the intervention they are randomized to.
 838 All participants will receive 300 KES (~\$2.70 USD) for their time and effort completing each study
 839 visit/questionnaire. For participants completing questionnaires remotely via the phone, we will send this
 840 reimbursement via a secured mobile money platform (i.e., M-Pesa), as we have done routinely for other
 841 projects. For participants that come to the PHRD research site to complete these visits/questionnaires in
 842 person, we will additionally provide reimbursement for transportation.

843 **DBS samples.** At follow-up (Month 3) DBS samples will be collected from peer clients to validate PrEP
 844 initiation. At a subset of in-person visits, a DBS collected from a finger prick or venous blood will be
 845 prepared at the site and stored at -20 degrees Celsius. Prior to storage, the DBS will be left to air-dry for
 846 at least 2 hours and thereafter placed in low gas-permeability Ziploc bags with a desiccant pack to reduce
 847 humidity thus maintaining integrity of the sample. The DBS samples will be labeled with the de-identified
 848 participant ID and will be shipped outside Kenya for temporary storage at Fred Hutchinson Cancer Center
 849 (Washington State, USA) and forwarded to Molecular Testing Labs (Washington State, USA) for TDF
 850 and FTC level testing. The shipped samples will be stored until the testing is completed and results
 851 confirmed. These outcomes are expanded on in the following section. It is possible that DBS samples
 852 will not be sent for testing if we do not achieve the target sample size of 23 peer clients per study arm.

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859 **Data Analysis**860 All outcomes will be measured at study follow-up (Month 3) (**Table. 8**).

Table 8. Outcomes for the peer PrEP referral + HIVST delivery trial, measured at 3 months. * = primary					Metrics of success: for R01 progression
Outcome:	Details:	Outcome type:	Reported:	Measures:	
PrEP initiation*	Prop. of clients initiating PrEP	Adoption (clients)	Provider	No. of new clients using PrEP / No. of referred clients	>20% increase
PrEP referral	No. of clients referred to PrEP	Adoption process (providers)	Provider	No. of clients referred to PrEP / No. of referred clients	>50 more peers
PrEP continuation ¹	Prop. of clients refilling PrEP (any) since referral	Adoption secondary (clients)	Provider	No. of clients with >1 PrEP clinic visits / No. of referred clients	>20% increase
PrEP continuation ¹	Prop. of providers refilling PrEP (any) in the past 3 months	Adoption secondary (providers)	Provider	No. of providers with 1+ PrEP clinic visits in past three months / No. of providers	>20% increase
PrEP adherence	Median of Wilson et al's 0-100 point adherence score	Adoption secondary (clients)	Client	Median score	>20% increase
HIVST use	Prop. of clients in the formal arm that used a HIVST.	Adoption process (clients)	Client	No. of clients self-reporting use of HIVST / No. of referred clients	≥90% (n=144 – formal arm)
Client linkage to care	Prop. of clients that went to a clinic to access HIV services	Adoption process (users)	Client	No. of clients reporting visiting a clinic / No. of referred clients	>20% increase
Recent HIV testing	Prop. of clients who completed any HIV testing since referral	Adoption secondary (clients)	Provider	No. clients reporting testing for HIV since referral/ No. of referred clients	>20% increase

¹Retention: >1 PrEP clinic visit (guidelines recommend first-time PrEP users return to a clinic after one month)

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Primary adoption outcome. Our primary outcome is reported PrEP initiation among all referred peer clients, as reported by peer providers (Objective 4). We had originally planned to measure this as a self-reported outcome among peer clients but had a challenge reaching peer clients that were referred in the pilot study; thus, have decided to link measurement of our primary outcome to peer providers delivering the intervention, as is typical in many studies assessing the impact of secondary distribution delivery models. To validate this, we will collect a DBS sample from a subset of willing peer clients that return in person at Month 3 (approximately 23/arm) to measure concentrations of tenofovir diphosphate (TFV-DP) and emtricitabine triphosphate (FTC-TP) using a validated liquid chromatography tandem mass spectrometry^{73,17}. Any concentrations of TFV-DP in a DBS sample will confirm PrEP initiation and/or adherence.¹⁶ In sensitivity analyses, we will measure our primary outcome using self-report data from peer clients (not providers) on PrEP initiation.

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Secondary adoption outcomes. We will also measure secondary and process outcomes of peer clients as reported by peer providers, including number of peers referred, recent HIV testing, and PrEP continuation (e.g., peer clients that returned to the clinic and refilled PrEP drugs one month following initiation). As in the primary analysis, we will measure these outcomes using reported data from peer clients (not providers) in sensitivity analyses. We will also measure some secondary and process outcomes of peer clients as reported by themselves, including PrEP adherence (measured using a standard scale), HIVST use, and linkage to care. Finally, we will also measure a secondary outcome of PrEP continuation among peer providers, as reported by themselves.

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Implementation outcomes. Additionally, in all follow-up surveys among peer providers and clients we will measure a number of implementation outcomes including participants' perceptions of the intervention's

882 acceptability, feasibility, and appropriateness. To measure these outcomes, we will use validated scales
 883 and established theories/frameworks adapted to the Kenyan setting and to young women (e.g., the
 884 Theoretical Framework of Acceptability). Additionally, at follow-up, we will have peer clients complete a
 885 checklist of materials received from peer providers to measure “fidelity” of the intervention in both
 886 intervention arms.

887 Costs are another important implementation outcome we plan on measuring during this trial. To measure
 888 costs, we will micro-cost the formal delivery model and compare the incremental cost of this model with
 889 the existing informal referral strategy (Objective 4). Activity-based micro-costing will be conducted for
 890 costs incurred (e.g., HIVST kits) and costs averted (e.g., personnel). We will use time and motion studies
 891 to measure staff time spent training peer providers. Estimates of cost using the activity-based approach
 892 will be compared with the top-down approach (i.e., the budget divided by the number of peer providers
 893 and peer clients)^{74 75 76 77} (**Table 9**).

894 **Safety.** We will measure “safety” of the intervention by
 895 screening for PrEP side effects (i.e., nausea, vomiting,
 896 headache) among peer clients (and as reported by both peer
 897 provider and clients) and any reports of social harm (e.g.,
 898 physical, verbal, emotional violence) related to our delivery
 899 model (Objective 4).

Table 9. Description of costing inputs

Costs: Start-up: microplanning, training, mobilization;

Recurrent: personnel, capital, supplies, overhead

Data: Project budget; time & motion; staff interviews;
published literature; central price list & salaries

Unit cost: Cost/PrEP users trained, peer referred, peer
initiated on PrEP, peer retained on PrEP.

900 The findings from this trial (described above) will be used to inform a NIH R01 proposal for a peer PrEP
 901 referral + HIVST community-randomized trial and budget impact analysis.

902 *Statistical analysis*

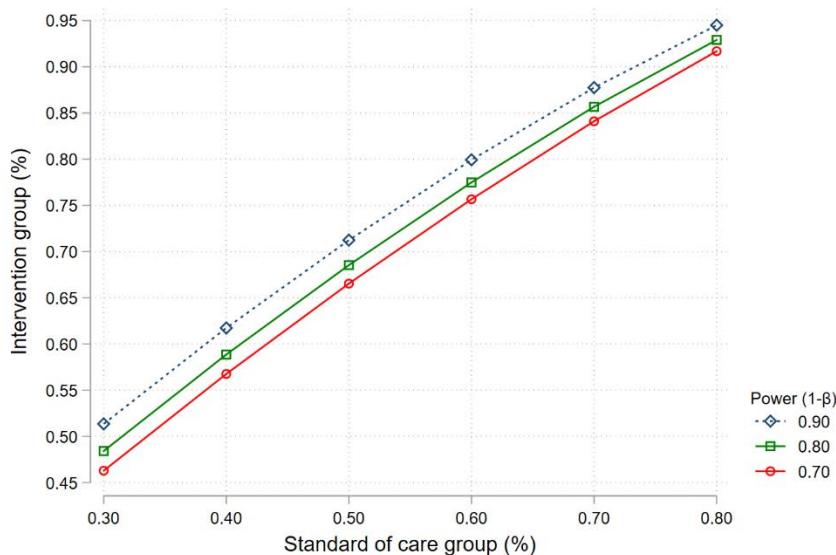
903 We will measure effect size estimates using mixed effects multilevel regression models (primary
 904 predictor: study arm; standard errors adjusted for clustering by peer provider). All analyses comparing
 905 randomization arms will be intention-to-treat, complete case analyses conducted at the unit of the
 906 individual (either peer provider or peer client). The primary comparison will be formalized peer PrEP
 907 referral + HIVST delivery versus informal peer PrEP referral (the standard of care). For analyses
 908 conducted at the level of the peer client, we will adjust standard errors for clustering at the peer provider
 909 level. We will use mixed-effect logistic regression models to measure risk ratios. All statistical test with 2-
 910 sided p-values <0.05 will be considered statistically significant. We will complete all analyses in R and
 911 STATA.

912 *Sample size*

913 If we assume that peer providers refer 75% of the targeted peer clients, this leaves us with three clients
 914 per peer provider, or 240 peer clients in total. We performed power calculations for our primary outcome,
 915 the proportion of referred peer clients who initiated PrEP at three months, in Stata 16.1 using methods
 916 for cluster-randomized trials, where each cluster is a peer group of one peer provider and three peer
 917 clients (**Figure 10**). **Table 10** shows the power we have to attain to detect various increases in the
 918 proportion of peer clients who initiated PrEP in the formal peer PrEP referral arm + HIVST (intervention
 919 group) vs. the informal peer PrEP referral arm (standard of care group). For our power calculations, we
 920 assumed 40 clusters (peer providers) per arm, 3 sampling units (peer clients) per cluster, and an intra-
 921 cluster correlation coefficient (ICC) of 0.05, which is standard for cluster-randomized controlled trials.
 922

925

Fig. 10. Power calculation to detect increase in the percentage (%) of referred peer clients initiating PrEP in the intervention group.



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Table 10. Increase in the % of referred peer clients initiating PrEP in the intervention group. ICC: 0.05; clusters (providers) per arm: 40; units (clients) per cluster: 3 (75% of suggested clients referred)

Power (%)	Standard of care (%), p1	Intervention (%), p2	Increase (%), p2-p1
70	30	46.3	16.3
	40	56.8	16.8
	50	66.5	16.5
	60	75.7	15.7
	70	84.1	14.1
	80	91.7	11.7
80	30	48.4	18.4
	40	58.9	18.9
	50	68.5	18.5
	60	77.5	17.5
	70	85.7	15.7
	80	92.9	12.9
90	30	51.4	21.4
	40	61.7	21.7
	50	71.2	21.2
	60	79.9	19.9
	70	87.8	17.8
	80	94.5	14.5

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Participant retention & withdrawal

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If we do not achieve our aim 1 pilot metrics of success (including our ability to follow-up with peers), we will revise the peer PrEP referral + HIVST delivery model with input from stakeholders before conducting the aim 2 trial. If necessary, we will try one of the alternative peer follow-up strategies outlined in aim 1, and in the worst-case scenario, we will have peer providers report peer client outcomes (an approach that has been used in other high-impact studies using peer-based health interventions⁷⁸). In the aim 2 trial, we will confirm self-reported PrEP initiation and adherence among a subset of peer clients with drug levels in DBS.

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Participants may voluntarily withdraw from the study for any reason at any time. The site investigators may also withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with required study procedures. Reasons for withdrawal will be recorded.

941 *PrEP discontinuation*

942 PrEP initiation and continuation will be in accordance with Kenyan PrEP guidelines. Use of PrEP may
943 be interrupted by the site investigators or Kenyan clinicians due to safety concerns for the participant or
944 use of concomitant medications that could interfere with PrEP or present a safety concern. All treatment
945 interruptions will be documented.

946

947 *Referral to continued PrEP care*

948 For participants that wish to continue PrEP care following the randomization trial, participants will remain
949 enrolled in PrEP at the healthcare facility at which they had enrolled in PrEP. PrEP will then be prescribed
950 and administered via this physician who will provide a 3-month supply of PrEP.

951 *PrEP drugs*

952 Tenofovir disoproxil fumarate (or TDF, 9-[(R)-2-[[bis [[(isopropoxycarbonyl) oxy] methoxy] phosphinyl]
953 methoxy] propyl] adenine fumarate), emtricitabine (or FTC, 5-fluoro-1-(2R,5S)-[2-(hydroxymethyl)-1,3-
954 oxatholan-5-yl]cytosine), and lamivudine (or 3TC, 2',3'-dideoxy-3'-thiacytidine 4-Amino- 1-[(2R,5S)- 2-
955 (hydroxymethyl)- 1,3-oxathiolan-5-yl]- 1,2-dihydropyrimidin- 2-one) are reverse transcriptase inhibitors
956 that have been approved for the treatment of HIV infection in humans in Kenya and the United States.
957 A fixed-dose, oral co-formulation of FTC/TDF (Truvada®) has also been approved for HIV prevention
958 in Kenya and the United States. The WHO recommends TDF-containing medications as PrEP, which
959 includes TDF combined with FTC as well as potentially TDF alone and TDF combined with lamivudine
960 (or 3TC, a medication closely related to FTC). Any TDF-containing medications that align with WHO
961 and Kenya national guidelines for PrEP will be used in this study. PrEP will be prescribed for once-daily
962 oral use. Study medication will be provided by the Kenyan MoH and stored in accordance with the drug
963 manufacturer's recommendations.

964 *HIVST kits*

965 ChemBio manufactures the SURE CHECK® HIV 1/2 Assay (**Fig. 6**), a blood-based HIVST that has
966 99.7% sensitivity, 99.9% specificity, presents results in 15 minutes, and is approved by the US FDA ³⁷.
967 Results are easy to interpret (1 line to indicate HIV-negative, 2 lines to indicate HIV-positive, and no lines
968 to indicate an invalid result). HIVST kits serve as a preliminary test result and must be followed-up with
969 confirmatory facility-based HIV testing to indicate a diagnosis. Additionally, we will use other WHO-
970 approved blood-based HIVST kits to mitigate supply chain or any other challenges that may arise.

971 *Limitations*

972 This randomization trial has some potential limitations that are important to note. Foremost, the trial will
973 encourage participants to recruit 4 peer clients to the study. The limitation of 4 peer clients may inherently
974 exclude some AGYW who have a high risk of HIV infection and would be interested in PrEP initiation
975 through a peer PrEP referral+ HIVST model. Further, peer clients recruited to the study and randomized
976 to the “formal peer PrEP referral + HIVST” arm, will be provided 2 HIVST kits to test themselves
977 (independently or with assistance from the participant) or to test a primary sexual partner. Some AGYW
978 may benefit from testing multiple sex partners (e.g., in sex worker relationships). Although a focus on
979 partner testing is outside the scope of this study, future research should be considered in this area.
980

981 Additionally, the randomization of participants to either the “formal peer PrEP referral+ HIVST” arm or the
982 “informal peer PrEP referral” arm may lead to feelings of frustration among participants who had hoped
983 to be randomized to the formal intervention delivery arm which may lead to resentment towards the
984 research team. Feelings of frustration are attempted to be mitigated by ongoing peer support (word-of-
985 mouth) to enroll in PrEP in the informal delivery arm.

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Finally, in the randomized trial, peers recruited to the study will be supplied HIVST kits free of cost. In settings outside of a research or intervention setting, AGYW will have to purchase HIVST kits at cost which may influence the feasibility of this model. The randomization trial aims to address this challenge by conducting a cost analysis which will be used to inform the design and development of a future peer PrEP referral + HIVST community randomization trial.

992 SAFETY**993 PrEP**

995 Multinational studies demonstrated that PrEP (including FTC/TDF) was safe for use in women from
996 Kenya and Uganda.²⁰ There were no statistically significant differences in the frequency of deaths,
997 serious adverse events, adverse events overall, or key laboratory adverse events (specifically, creatinine
998 elevation and phosphorus decrease) for those receiving PrEP compared to those receiving placebo in
999 the Partners PrEP Study.

1000 For the purposes of this study, only serious adverse events (SAEs) will be documented. SAEs felt to be
1001 related to PrEP will result in temporary hold of PrEP. In the case of temporary holds, the hold will continue
1002 until the event is stabilized or resolved. If the event resolves, PrEP may be reinitiated at the discretion of
1003 the Data Monitoring Committee (see "Study oversight" below), resuming safety monitoring. The severity
1004 of clinical symptoms will be scored using the Division of AIDS- NIH (DAIDS) Table (July 2017 Version)
1005 for Grading the Severity of Adult and Pediatric Adverse Events (AEs). Reporting on adverse events to
1006 relevant IRBs will be according to relevant regulations.

1007 Pregnancy

1008 Animal and human data, including from the Partners PrEP Study and Partners Demonstration Project,
1009 suggest safety of FTC/TDF when used by HIV infected women during pregnancy and breastfeeding.
1010 Other studies are exploring detailed safety of PrEP use in pregnancy. For this study, pregnant women
1011 interested in PrEP will be referred to antenatal care clinics for PrEP initiation and refills, as caring for a
1012 woman who is pregnant and on PrEP is outside of the scope of this study.

1013 Social harm considerations

1014 We have extensively considered the risk of social harms related to both PrEP use and peer referral to
1015 PrEP as well as peer HIVST delivery including risks of depression/anxiety and disclosure and stigma.
1016 Our extensive experience with longitudinal follow-up of heterosexual HIV sero-discordant couples and
1017 women at risk mitigates some of this risk, and we found very little risk of social harms or anxiety related
1018 to HIV self-testing from our ongoing Pharmacy PrEP study. Analyses of social harm related to peer PrEP
1019 referral + HIVST will be by relationship status and employment status/type, given the potential for
1020 differential employment and relationship risks. In the event of a clinical need (e.g., side effects, symptoms
1021 of a sexually transmitted infection), participants will be referred to nearby HIV clinics for care.

1022 **HUMAN SUBJECTS CONSIDERATIONS**

1023 The protocol, informed consent forms (for pilot participation, for focus group discussions, and for the
 1024 randomization trial), and patient education and recruitment materials will be reviewed and approved by
 1025 the institutional review boards at the Fred Hutchinson Cancer Center and the Scientific Ethics Review
 1026 Unit (SERU) at the Kenya Medical Research Institute (KEMRI). All participants will provide informed
 1027 consent before participation in the pilot study and randomization trial. Participants will be informed of the
 1028 purpose of the study, the procedures to be followed and the risks and benefits of their participation. The
 1029 consents forms will be translated into Kiswahili. Specifically, the participants will be informed that this
 1030 novel study will answer critical questions on acceptability, feasibility, and facilitators/barriers to a model
 1031 of peer PrEP referral + HIVST among AGYW in Kenya.

1032 **Study oversight**

1033 This study will be subject to oversight by an independent Data Safety Monitoring Committee that will
 1034 periodically review data from the study, including study execution, adherence, HIV incidence, PrEP side
 1035 effects, SAEs, and social harms by study arm. Adverse events (AEs) include any forms of verbal (e.g.,
 1036 yelling, fighting), physical (e.g., hitting), emotional (e.g., depression) or economic (e.g., job loss) abuse.
 1037 While serious adverse events (SAEs) include hospitalization (for any condition, including those outside
 1038 the study) or death. During data collection and study follow-up, participants will be asked to report if
 1039 they've had any of these events and whether they are or are not study related. We have had a Data
 1040 Monitoring Committee for many of our other ongoing studies. The independent data monitoring
 1041 committee will provide recommendations to the study team as part of periodic reviews. Reports from all
 1042 reviews will be provided for submission to overseeing IRBs and Ethics Committees (ECs).

1043 **Risks**

1044 Participants may become embarrassed, worried, or anxious when completing their HIV risk assessment
 1045 and/or receiving HIV counseling at healthcare facilities for PrEP enrollment. They also may become
 1046 worried or anxious while waiting for their HIV test results following HIV self-testing. Participants who learn
 1047 that they have HIV may experience anxiety or depression related to their test results. Further, participants
 1048 may become embarrassed or worried when they approach peers about PrEP, encourage peers to
 1049 HIVST/assist peers to HIVST, or when they disclose their HIV status and/or PrEP use to peers (should
 1050 they choose to do so). At all study sites, individual counseling will be provided by researchers who have
 1051 been trained in specific issues related to HIV risk, HIV prevention, HIV acquisition, and HIV treatment.

1052 Although study sites will make every effort to protect participant privacy and confidentiality, it is possible
 1053 that participants' involvement in the study could become known to others, particularly as this project will
 1054 utilize a peer-delivered model. There is a possibility that social harms may result (i.e., because
 1055 participants could become known as participating in studies involving HIV prevention). For example,
 1056 participants could be treated unfairly, stigmatized, or discriminated against, or could have problems being
 1057 accepted by their families and/or communities. Talking about HIV or PrEP and finding out HIV test results
 1058 could cause problems between a participant and their sexual partner(s), including the potential for
 1059 intimate partner violence (e.g., any physical, verbal, emotional, or economic harm). Understanding the
 1060 risk/benefit balance for confidential delivery of PrEP services in community settings is an explicit goal of
 1061 this project. Moreover, we have extensive experience with the strategies to minimize the potential for
 1062 social harms in populations participating in HIV prevention studies.

1063 Risks and side effects related to PrEP include gastrointestinal intolerance and rarely more serious side
 1064 effects; these are detailed on the package insert and this project is not testing PrEP itself but its delivery.
 1065 The medical risks of HIV testing using blood collection are small.

1066 **Protection against risk**

1067 The study team has extensive experience with counseling about HIV risk, PrEP, HIVST, and strategies
 1068 for HIV prevention in general. Study procedures will include quantitative surveys (e.g., PrEP initiation,
 1069 peer PrEP referral) as well as qualitative interviews to understand acceptability of the model. PrEP will
 1070 be provided at specified healthcare facilities and will follow Kenyan clinical guidelines. Counseling about
 1071 antiretroviral-based HIV prevention will include messaging describing the benefits of all strategies, based
 1072 on evolving available data and national policies / national roll-out of antiretrovirals (including earlier
 1073 treatment and PrEP) for HIV prevention.

1074 For data collection, standardized questionnaires will be used that will include questions on sensitive
 1075 topics, including sexual behavior, depression, alcohol use, and stigma. We have extensive experience
 1076 with these questionnaires from our prior studies and the expertise and counseling resources required to
 1077 attend to study participants (e.g., those with depression). We have published on very low rates of social
 1078 harm and intimate partner violence in our prospective studies of HIV sero-discordant couples, which likely
 1079 reflects the counseling available to couples; for women at risk, we have extensive experience with
 1080 management of potential social harms, through our prevention studies.

1081 To minimize risks to minors, we will only enroll young women ≥ 16 to 17 years into the study if they are
 1082 emancipated minors and thus able to legally provide consent for participation in research. Kenyan law
 1083 acknowledges women ages 14 to 17 who have become pregnant as emancipated minors. We have
 1084 successfully enrolled emancipated minors into a number of prior studies, including PrEP clinical trials. In
 1085 addition, Kenya national policy guidelines explicitly permit PrEP use in this age group.

1086 The risks from the anticipated activities will be no greater than in our previous studies; in fact, given the
 1087 proven prevention benefits of PrEP and its national roll-out in Kenya, risks are anticipated to be less than
 1088 in some of our prior studies. We feel the risks associated with the study are small. The benefits are
 1089 consistent with clinical care benefits and cultural expectations, and they follow the established standard
 1090 with IRB approval in our other studies. We therefore believe the balance of benefit and risk is appropriate.

1091 **Benefits**

1092 All participants will have the benefit of using novel HIVST kits, which are being scaled-up by the Kenyan
 1093 Ministry of Health. Further, participants will have the added benefit of pioneering a combined peer PrEP
 1094 referral and HIVST model. HIV prevention practices, according to national guidelines, will be provided to
 1095 all participants enrolled in this study. This will include risk reduction counseling, addressing sexually
 1096 transmitted infections, and access to condoms. In addition, participants and others may also benefit in
 1097 the future from information learned from this study. There may be no other direct benefits to participants
 1098 in this study.

1099 **Care for persons identified as HIV infected**

1100 This study may identify persons who are infected with HIV, either as part of the study screening process
 1101 (e.g., when peers utilize HIVST) or during follow-up of enrolled participants. Study staff will provide
 1102 participants with their HIV test results in the context of post-test counseling. Persons identified as HIV
 1103 infected during the study screening process, and who do not meet eligibility criteria will be referred to
 1104 nearby clinics where they can receive free HIV care and treatment services. For participants who are HIV
 1105 infected and who also become pregnant during follow-up, every effort will be made to facilitate access to
 1106 programs for preventing mother-to-child HIV transmission for appropriate antiretroviral treatment to
 1107 reduce the probability of HIV transmission from mother to child.

1108 **Benefits to the community**

1109 An important goal of this study is to achieve the study objectives in a way that provides benefits to the

1110 community that endure beyond the proposed study lifetime regardless of the specific outcome of the
1111 study. Some of these community benefits include development of optimized approaches to HIV
1112 prevention care and community awareness of comprehensive HIV prevention.

1113 **Importance of the knowledge to be gained**

1114 Knowledge gained from the studies proposed in this application will include information about optimal
1115 delivery of PrEP for HIV prevention among a vulnerable group (e.g., AGYW), which may have substantial
1116 impact on the global burden of HIV.

1117 **Treatment for injury**

1118 Participants will be asked to inform the clinic staff if they feel they have been injured because of taking
1119 part in the study. Injuries may also be identified during laboratory testing, medical histories, and physical
1120 examinations at the specified healthcare facilities where participants will have access to PrEP. Treatment
1121 for adverse events related to study participation will be provided by the treatment clinic. If treatment is
1122 required that is beyond the capacity of the clinic, the clinic staff will refer the participant to appropriate
1123 services or organizations that can provide care for the injury. Participants will be financially responsible
1124 for treatment for injuries.

1125 **Study records**

1126 Implementation investigators will maintain, and store in a secure manner, complete, accurate, and current
1127 study records throughout the study. Study records include administrative documentation and regulatory
1128 documentation as well as documentation related to each participant enrolled in the study, including
1129 informed consent forms, data forms, notations of all contacts with the participant, and all other source
1130 documents.

1131 **Confidentiality**

1132 Every effort will be made to protect participant privacy and confidentiality to the extent possible. Personal
1133 identifying information will be retained at the local study sites and not forwarded to Fred Hutch. The sites
1134 will use their standard operating procedures for confidentiality protection that reflects the input of study
1135 staff and community representatives to identify potential confidentiality issues and strategies to address
1136 them.

1137 All study-related information will be stored securely at the study sites. All participant information will be
1138 stored in areas with limited access. Data collection, administrative forms, and other reports will be
1139 identified only by a coded number to maintain participant confidentiality. All records that contain names
1140 or other personal identifiers, such as locator forms and informed consent forms, will be stored separately
1141 from study records identified by code number. All local databases will be secured with password-
1142 protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link
1143 participant ID numbers to other identifying information will be stored in a separate, locked file in an area
1144 with limited access. During FGDs, we will ask participants not to refer to each other by name. During the
1145 peer providers trainings, we will instruct peer providers to not enter any identifying information about peer
1146 clients in the WhatsApp group messages. Any personal identifiers will be removed from the qualitative
1147 data transcripts and immediately deleted from WhatsApp messages by the study team. Recordings will
1148 be destroyed at the end of the study. WhatsApp group messages will not be stored long term (they will
1149 be periodically deleted), and the WhatsApp groups will be shut down at the end of the intervention period
1150 for each group of peer providers in the intervention arm.

1151 **Dissemination Plan**

1152 The study team is committed to the public dissemination of results from the pilot study and the

1153 randomization trial to participants, local stakeholders in Kenya, the global scientific community, and U.S.,
1154 Kenyan, and global policymakers. Dissemination of study results will follow principles of good
1155 participatory practice. Results will be published in conference abstracts and peer-reviewed journals.
1156 Study results will be disseminated through presentations to local stakeholders and policymakers in
1157 Kenya, including the Ministry of Health.

1158 **TIMELINE**

1159 The findings from the pilot study and randomization trial will provide important information on how to
 1160 increase PrEP initiation and continuation among young women at HIV risk in Kenya, which can inform
 1161 Kenya MOH guidelines around PrEP delivery. Additionally, these findings will inform the development of
 1162 an R01 proposal for a community-randomized trial and budget impact analysis of peer PrEP referral +
 1163 HIVST delivery in Kenya, should aims 1 & 2 find the delivery model promising among young women
 1164 (**Table 11**).
 1165

Table 11. Timeline and outcomes		R00 phase: Y1 Y2 Y3		
Aim 1: Pilot	Protocol prep. & IRB submission	X		
	Pilot & refine Aim 1 delivery model	X		
	Conduct & analyze FGDs	X		
	Manuscript(s) preparation	X		
Aim 2: Randomization Trial	Protocol prep. & IRB submission	X		
	Enrollment, data collect, analysis	X	X	X
	Collect & analyze costing data		X	X
Planned R01 submission (Community Randomization Trial)				X

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