Study Overview

Brief Summary

A randomized, crossover study to compare adherence, preference and acceptability of an over-encapsulated dual prevention pill (DPP capsule) containing oral pre-exposure prophylaxis (PrEP) and a combined oral contraceptive (COC) versus two separate tablets (PrEP and COC) among women at risk of HIV and unintended pregnancy in Johannesburg, South Africa

Detailed Description

SOUTH AFRICA We will conduct a randomized, open-label, parallel group, 2-way crossover study among approximately 96 women aged 16-40 years old to compare adherence, preference, acceptability and safety of a single dual prevention pill (DPP) containing Truvada and the generic COC, Zinnia F (Regimen A), versus Truvada and Zinnia F taken separately (Regimen B). All participants must already be using COCs for at least 3 months prior to screening and must plan to continue using them for at least one year. We are enrolling women who are already using COCs because we believe they are most likely to be interested in a daily oral MPT. Furthermore, we would like participants who are already accustomed to COCs so that they can have a clearer sense of how PrEP - whether taken separately or in the DPP - makes them feel.

Prior to the commencement of the study, the Population Council procured and qualified all study drugs required for the crossover study, including: bulk pills (Truvada and Zinnia F) for encapsulation, COC pill packs, and bottles of Truvada. Under the guidance of the Council's clinical and regulatory groups, PCI Pharma (Rockford, IL, USA) over-encapsulated Truvada and Zinnia F according to Good Manufacturing Practices. The over-encapsulated pills were then blister packaged, pouched, and kitted for distribution to participants.

The DPP regimen (A) consists of a kit containing 4 pouches with a 28-day supply of over-encapsulated pills; 21 pink and white capsules will contain Truvada over-encapsulated together with a COC; the other 7 capsules, corresponding to the 7 placebo days in a COC pill pack, will be white and will contain Truvada only. The provider counseling manual will emphasize the fact that unlike a COC pill pack where 7 pills are placebo, all of the pills in the regimen contain Truvada, so it will be important to take them for all 28 days. For Regimen B, participants will receive a 28-day blister pack of Zinnia F, as is currently marketed, with 21 active pills and 7 placebo pills. Truvada will be dispensed in bottles of 30 pills, as is currently marketed. Participants will be instructed to take one Truvada tablet and one COC table daily for 28 days.

After providing written informed consent (or assent, with parental consent, for 16-17-year-old girls), women will be screened for eligibility. Participants can be enrolled if they are sexually-active (defined as

having had penile-vaginal sex with a male ≤3 months before screening), currently using a COC that was started ≥3 months before screening, HIV-negative (based on HIV rapid test at screening), not-pregnant (based on hCG urine test at screening), have no contraindications for PrEP or COCs, and are in good health based on medical history and vital signs. PrEP screening will follow the standard of care in South Africa, which recommends testing for Hepatitis B, blood creatinine levels, pregnancy, and STIs. Women who test positive for pregnancy or HIV will be referred per the local standard of care. Participants who test positive for a curable STI will be treated and enrolled. Participants who are eligible will be scheduled for an enrollment visit on Day 0 of their menstrual cycle.

At enrollment, women will be randomly assigned to one of two sequences of the two regimens, with all women using both regimens by the end of the crossover study. The Population Council study biostatistician created the randomization scheme using Statistical Analysis Software (SAS/STAT) version 9.4 (SAS Institute Inc., Cary, North Carolina) with a 1:1 allocation using permutated block sizes. Randomization is in blocks of 12, with 6 participants assigned to each sequence in each of 8 blocks. Half of the women will be assigned to Sequence 1, which is Regimen A followed by Regimen B and the other half will be assigned to Sequence 2, which is Regimen B followed by Regimen A. Participants will use each regimen for 3 28-day menstrual cycles and will then switch to the second regimen at their crossover visit. At the end of the crossover period, participants will be offered a choice of Regimen A or Regimen B (or neither) to use for up to an additional 6 months.

Participants will attend a total of up to 14 clinic visits including Screening, Enrollment and monthly follow up visits for up to 12 months. No wash-out period is required between regimens. At Visit 1, prior to initiating product use, participants will be asked to complete a baseline behavioral interview and will be asked which regimen they think they will prefer. At all other visits, participants will complete behavioral interviews (approximately 30 minutes) about adherence and acceptability. All behavioral interviews will be conducted using computer assisted self-interviewing (CASI), which has been shown to elicit more truthful reporting than face-to-face interviewing. At the end of the Crossover period, participants will complete their final CASI interview, in which they will be asked to 1) state their preference for the DPP or 2 separate pills; 2) to qualify the strength of their preference on a scale of 1-10; and 3) to respond to questions about why they selected one regimen over the other (or not). A subset of participants who complete the study and anyone who withdraws early will be asked to take part in an in-depth interview to explore qualitatively reasons for continuation and discontinuation, as well as the influence of partners, family, support structures, side effects, provider interactions and other factors on cMPT choice and adherence.

At all follow up visits, women will be tested for HIV and pregnancy, report adverse events (AEs) and have a clinical exam, if necessary, and respond to a structured questionnaire via computer assisted self-interview (CASI) with questions about acceptability, preference, and adherence. At the end of the Crossover period, women will be asked to state which regimen they prefer. Accrual is estimated to take approximately 17 months from first participant enrolling to last participant completing the study. We will assess and compare PrEP acceptability and adherence by regimen and overall, and we will investigate if specific socio-ecological factors (e.g., individual-, partner-, family-, and clinic-level) are associated with adherence and acceptability. We will also explore facilitators and barriers to use by conducting in-depth interviews with a subset of willing participants who complete the study and any

women who withdraws early. Furthermore, because we assume people are predisposed to judge a specific regimen or technology based on initial impressions, we will assess if pre-use preferences are associated with actual experiences and preferences after using each regimen.

At each visit, women will be tested for pregnancy and HIV and will provide a blood sample for DBS to assess drug levels/adherence to PrEP. Adverse events will be recorded during the study, although no pharmacokinetic interactions are expected because there are no drug-drug interactions between the reverse transcriptase inhibitors tenofovir and emtricitabine, and the contraceptive hormones levonorgestrel and ethinyl estradiol. In addition, the side effects profiles of the two products are similar; the most commonly reported side-effects for both Truvada® and COCs are headache and nausea. Since we are recruiting women who are already using COCs, participants will already be accustomed to side-effects of COCs. Participants will be encouraged to contact or visit the clinic with questions or concerns between visits.

Rapid HIV testing will be done at screening, in accordance with local guidelines. Pregnancy will be tested based on hCG levels in urine. DBS collected from enrolled participants will be sent to the University of Cape Town where tenofovir disoproxil fumarate (TDF) drug levels will be measured to evaluate adherence based on expected levels for daily use.

Quantitative and qualitative behavioral collection instruments will adhere to our theoretical framework for assessing acceptability, with questions adapted from previous HIV-prevention studies, as relevant. In-depth interview guides will be developed from instruments used in previous PrEP introduction studies and tailored for this study.

Quantitative data from the CASI behavioral interviews will be saved at the site in .csv (comma separated value) format and shared with Population Council weekly via encrypted zip files. Clinical data collected from participants, including background demographics; medical and pregnancy history; vital signs; concomitant medications; AEs; enrollment and termination dates; and records of returned unused pills will be entered into REDCap, an electronic data system. Data from CASI interviews, eCRFs and DBS analysis will be formatted into SAS data sets for analysis. Descriptive statistics (frequencies, mean, standard deviation, range) will be used to summarize data collected and to characterize differences in participants assigned to each Sequence. Modeling will be used to assess the impact of background characteristics on adherence, preference and acceptability.

PC conducted site initiation and training for the crossover study in collaboration with Wits RHI, which has extensive experience implementing qualitative and quantitative HIV prevention research studies. The Population Council and site coordinator have weekly teleconferences and the full teams are meeting monthly during data collection to discuss and resolve any issues as they occur. The PC clinical research associate will make periodic monitoring trips during data collection to ensure the safety of participants and adherence to the protocol. The PC team will also review data collected on a weekly basis.

Official Title

A Randomized, Crossover Study Comparing Adherence, Preference + Acceptability of a Dual Prevention Pill (DPP) Capsule Containing PrEP + an Oral Contraceptive Versus Two Separate Pills in Women at Risk of HIV in Johannesburg, South Africa

Conditions

HIV Infections

Intervention/Treatment

- Drug: Dual Prevention Pill
- Drug: PrEP tablet and a COC as two separate tablets

Other Study ID Numbers

- Protocol #953

Study Start (Actual)

2022-09-13

Primary Completion (Estimated)

2024-01-31

Study Completion (Estimated)

2024-01-31

Enrollment (Actual)

96

Study Type

Interventional

Phase

Not Applicable

Resource links provided by the National Library of Medicine

MedlinePlus (https://medlineplus.gov/) related topics: HIV (https://medlineplus.gov/hiv.html) HIV and Pregnancy (https://medlineplus.gov/hivandpregnancy.html)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

This study has 1 location

South Africa

Gauteng Locations

Johannesburg, Gauteng, South Africa, 2001
Witwatersrand Reproductive Health & HIV Institute's (WITS RHI)

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

1. Age 16 through 40 years old (inclusive) at Screening, verified per site-specific SOPs.
2. Able and willing to provide informed consent per site SOPs. (If under the legal age of consent [18 years old] be able to provide informed assent and obtain parental or guardian consent, to be screened for and to enroll in the study.)
3. Fluent in spoken Zulu and/or English.
4. Able and willing to provide adequate locator information, as defined in site SOPs.
5. Able and willing to comply with all study procedures, including being comfortable taking the study products as evident by nurse/clinician-observed swallowing at Screening of a large Vitamin capsule that is of similar size to the study products.
6. Post-menarche, per participant report at Screening.
7. Sexually active, defined as having had penile-vaginal sex with a male within the 3 months before Screening (per self-report).
8. At moderate to high risk of HIV infection based on clinician assessment.
9. Considers herself to be at moderate to high risk of HIV acquisition based on self-assessment.
10. Has been using COCs for contraception for at least 3 months prior to Screening as confirmed by contraceptive card and intends to continue using COCs for at least 12 months.
11. HIV-negative per rapid test at Screening and Enrolment per site-specific SOP.
12. Negative pregnancy test at Screening and Enrolment.
13. Negative for chlamydia, gonorrhea, trichomoniasis, and syphilis at Screening; women who test positive at Screening may be treated and enrolled.
14. Hepatitis B surface antigen (HBsAG) negative per blood test at Screening.
15. Normal estimated creatinine clearance (eCrCl) ≥ 60 ml/min per blood test at Screening.

Exclusion Criteria:

1. Intends to become pregnant within the next 12 months.
2. Intolerance, adverse reaction, or laboratory abnormality associated with PrEP use in the past.
3. Use of PEP within 3 months of Screening (per self-report).
4. Breastfeeding < 6 months postpartum (per self-report).
5. Less than 6 weeks (≤42 days) postpartum and not breastfeeding (per self-report).
6. For women 35 and older, currently smokes cigarettes (self-report).
7. History of deep vein thrombosis / pulmonary embolism (self-report) or history of thrombophlebitis or thromboembolic disorders at Screening (per self-report or medical records).
8. Prolonged immobilization (self-report).

9. Known thrombogenic mutation/complicated valvular disease (per self-report).
10. Ischemic heart disease (per self-report).
11. Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies (per self-report).
12. Migraines with aura
13. For women over 35 years old, migraines without aura (per self-report).
14. Current breast cancer or within 5 years of past breast cancer (per self-report) or history of carcinoma of the breast or other estrogen-dependent neoplasia reported at Screening.
15. Diabetes with nephropathy, retinopathy, or neuropathy (per self-report).
16. Diabetes for > 20 years (per self-report).
17. Symptomatic gall bladder disease (per self-report).
18. Severe cirrhosis (per self-report).
19. Liver tumor (per self-report).
20. Any other condition the clinician feels would jeopardize the health and wellbeing of the participant.

Ages Eligible for Study

16 Years to 40 Years (Child, Adult)

Sexes Eligible for Study

Female

Accepts Healthy Volunteers

Yes

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Randomized
Interventional Model : Crossover Assignment
Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Over-encapsulated DPP A single, over-encapsulated DPP taken once daily for three 28-day cycles (Regimen A) followed by two separate tablets (oral PrEP and COC) taken once daily for three 28-day cycles (Regimen B)	Drug: Dual Prevention Pill • a single over-encapsulated DPP containing a PrEP tablet and a COC • Other Names: ◦ DPP

Experimental: Two Separate Tablets
 	
Two separate tablets (oral PrEP and COC) taken once daily for three 28-day cycles followed by a single, over-encapsulated DPP taken once daily for three 28-day cycles
	Drug: PrEP tablet and a COC as two separate tablets
	
	• PrEP tablet and a COC as two separate tablets
	
	• Other Names:
	  ◦ Truvada
	
	  ◦ Zinnia F

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
To compare adherence to the DPP capsule (Regimen A) versus 2 separate tablets (Regimen B) among women using each regimen daily for 3 28-day menstrual cycles during the Crossover period.	TFV-DP levels in dried blood spots (DBS) by regimen, and overall, at follow up visits every 4 weeks during Crossover period.	At the end of Cycle 3 (each cycle is 28 days)
To compare adherence among women who choose the DPP capsule (Regimen A) versus adherence among women who choose 2 separate tablets	TFV-DP levels in DBS by regimen, and overall, at follow up visits every 4 weeks during Choice period.	At the end of Cycle 3 (each cycle is 28 days)

(Regimen B), each taken daily during the Choice period.		
To assess and compare self-reported adherence to Regimen A vs Regimen B during the Crossover period, and to the chosen method during the Choice period.	Self-assessment of ability to adhere to instructions for product use (DPP capsule, FTC/TDF and COCs as applicable) in CASI interviews at follow up visits every 4 weeks during the Crossover and Choice periods.	Monthly for up to 48 weeks
To assess and compare adherence to Regimen A vs Regimen B during the Crossover period, and to the chosen method during the Choice period based on pill count.	Proportion of doses taken vs expected by pill count (DPP capsule, FTC/TDF and COCs as applicable) at follow up visits every 4 weeks during the Crossover and Choice periods.	Monthly for up to 48 weeks
To determine preference for taking a single DPP capsule	Proportion of women who prefer the DPP (Regimen A) vs 2 separate tablets (Regimen B) after using each regimen for 3 28-day cycles,	At the end of Cycle 3 (each

versus 2 separate tablets (PrEP and COC) once daily among women after using each regimen for three 28-day cycles.	per self-report on computer-assisted self-interviewing (CASI).	cycle is 28 days)
To determine if more women choose Regimen A versus Regimen B for the Choice period.	Proportion of women who choose Regimen A vs B for the Choice period.	At the end of the Crossover period (6 months)

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
To compare the safety of Regimen A versus Regimen B among women using each regimen for 3 28-day cycles during the Crossover period, and the	Number of AEs by regimen (including social harms, drug side effects) during the Crossover and Choice periods.	Monthly for up to 48 weeks

safety of Regimen A versus Regimen B among women choosing each regimen during the Choice period.		
To explore facilitators and barriers to use, as well as socio-ecological factors that may be associated with adherence.	Results of multivariate modeling indicating which, if any, factors are associated with adherence.	Monthly for up to 48 weeks
To assess the acceptability of the DPP vs 2 separate tablets taken daily to prevent HIV and unintended pregnancy among women using each regimen for 3 28-day cycles during the Crossover period, and for up to 6 28-day	Scores by regimen and overall, as measured in a quantitative acceptability questionnaire via CASI at the Crossover visit, the start of the Choice period, and the end of the study.	3 months, 6 months, 12 months

cycles during the Choice period.		
To assess if pre-use opinions are associated with actual experiences and preferences after using each regimen.	Proportion of women whose pre-use preference matches post-use experience based on a CASI questionnaire at baseline and at the end of the Crossover period.	Baseline and end of Crossover (6 months)
To qualitatively understand barriers and facilitators to product use and adherence.	Results of thematic qualitative data analysis from in-depth interviews with participants at study exit focusing on facilitators and barriers of product use and adherence.	through study completion, an average of 48 weeks
To explore if socio-ecological factors, product characteristics and product use experiences are associated with acceptability of the DPP and of 2 separate tablets.	Results of multivariate modeling indicating which, if any, factors are associated with acceptability.	3 months, 6 months, 12 months

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Population Council

Investigators

- Study Director: Barbara Friedland, MPH, Population Council

Publications

From PubMed

These publications are automatically filled in from PubMed, a public database of scientific and medical articles, and may or may not be about the study.

- Ndlovu N, Plagianos M, Palanee-Phillips T, Reddy K, Zulu SK, Kgoa RFO, Irene B, Shale LR, Burnett-Zieman BJ, Sigcu NS, Mathur S, Haddad LB, Friedland BA. Adherence, Preference, and Acceptability of an Overencapsulated Dual Prevention Pill for HIV and Pregnancy Prevention Among Women in Johannesburg, South Africa. J Acquir Immune Defic Syndr. 2026 Feb 1;101(2):141-152. doi: 10.1097/QAI.0000000000003780. (https://pubmed.ncbi.nlm.nih.gov/41526807)

- Friedland BA, Mgodi NM, Palanee-Phillips T, Mathur S, Plagianos MG, Bruce IV, Lansiaux M, Murombedzi C, Musara P, Dandadzi A, Reddy K, Ndlovu N, Zulu SK, Shale LR, Zieman B, Haddad LB. Assessing the acceptability of, adherence to and preference for a dual prevention pill (DPP) for HIV and pregnancy prevention compared to oral pre-exposure prophylaxis (PrEP) and oral contraception taken separately: protocols for two randomised, controlled, cross-over studies in South Africa and Zimbabwe. BMJ Open. 2024 Mar 12;14(3):e075381. doi: 10.1136/bmjopen-2023-075381. (https://pubmed.ncbi.nlm.nih.gov/38479746)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted

2021-02-25

First Submitted that Met QC Criteria

2021-02-26

First Posted

2021-03-03

Study Record Updates

Last Update Submitted that Met QC Criteria

2024-02-01

Last Update Posted

2024-02-06

Last Verified

2024-02