Multipurpose Prevention Technologies: HPTN 104

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EVERY MINUTE

Approximately:
• 230 unplanned pregnancies
• 140 abortions
• 3 infected with HIV
• 1 HIV/AIDS-related death

Every 2 minutes
• 1 maternal death

Global Need: Overlapping Risks

1.5 million acquired HIV in 2020

~40% all pregnancies are unintended

Over 1 million people contract a sexually transmitted infection every day
Current HIV/STI Prevention Options have Limited Potential and Do Not Address the Needs of Many Women
Studies Show Women Want MPTs

- 83% of 18-29 year old women (n=835) in an online U.S. Mturk survey were interested in MPTs (Hynes)

- 96% of women (n=225) in TRIO study a product for HIV and pregnancy prevention versus 2 separate products (Minnis)

- 82% of women (n=640) in the Share.Learn.Shape online survey preferred an HIV/STI prevention product with contraception versus disease prevention alone (Friedland)
Multiple Benefits of MPTs

- **Women's Health**
  - ↓ Maternal Deaths, Unsafe Abortion
  - ↓ STIs, pelvic pain, cancer and infertility
  - ↓ Pregnancy Complications
  - ↓ HIV/AIDs

- **Empower**
  - ↓ Teen Pregnancy
  - ↓ Birth Spacing
  - ↓ Preterm birth and low birth weight
  - ↓ Mother-to-child transmission
  - ↓ Under-5-mortality

- **Education**
  - ↑ Women’s earning capacity
  - ↑ Age at First Birth
  - ↑ Number of Years in School

- **Economic Benefit**
  - ↑ Birth Spacing
  - ↑ Number of Years in School
  - ↑ Economic development
  - ↑ Income and assets

- **Child Health**
  - ↓ Teen Pregnancy
  - ↓ Preterm birth and low birth weight
  - ↓ Mother-to-child transmission
  - ↓ Under-5-mortality

- **Health care costs**
  - ↓ Days of work missed

- **MPTs**
  - ↑ Birth Spacing
  - ↓ Preterm birth and low birth weight
  - ↓ Mother-to-child transmission
  - ↓ Under-5-mortality

- **Other STIs**
  - ↑ Women’s earning capacity
  - ↑ Age at First Birth
  - ↑ Number of Years in School

- **Income and assets**
  - ↑ Economic development
  - ↑ Income and assets
Multiple reasons for wanting an MPT

- Discreet
- Control
- Convenient
- Easier to adhere
- Greater acceptability

- Overcome stigma
- Enhancing sex
- Improving sex for partner
- Minimize clinic visits
- Autonomy

GOAL

To decrease HIV incidence via increasing optimal PrEP use and enhance choice for people of childbearing potential
MPT development/introduction framework

Positioning MPTs within the Current Contraceptive Landscape

- Effectiveness
- Control
- Side Effects
- Secondary Benefits
- Shared Decision-making
MPT Products in Development:
A focus on choice, convenience and control

Provider administered
- Implants
- IUDs

User controlled
- Daily oral tablets
- Intravaginal rings
- Patch
- Films, gels, inserts

Characteristics of APIs and Regimens
- Long-acting, short-acting, on demand
- Hormonal/non-hormonal contraceptive
- ARV vs non-ARV
- Systemic (absorbed in blood) vs topical
- Approved vs novel
Dual prevention pill (DPP)

Streamlined regulatory pathway: no efficacy trials required, only bioequivalence

WHO/CDC guidelines recommend PrEP and combined oral contraceptives prescribed together
Promise of the DPP
Findings from formative acceptability studies

• Ease of Use
  • Lessen the burden of taking two pills
  • Result in fewer clinic visits for women currently using both PrEP and COCs

• Control
  • Autonomy in preventing HIV and pregnancy
  • Quick return to fertility

• Enhanced protection for unprotected/condomless sex

I think it’s good because the pills will not be too many for you, you would know that you take one (pill) for both unlike taking this one and then you take another one.

Zimbabwe

Like if the male partner tested HIV-positive, he has HIV and wants to sleep with you by force he won’t be able to infect you because you are taking the DPP.

South Africa

Source: focus group discussions: 16–40 women from South Africa and Zimbabwe (14 FGDs, 104 participants)

Potential Challenges of the DPP
Findings from formative acceptability studies

- **Product**
  - Side effects
  - Daily dosing, difficulty swallowing

- **Service provision**
  - Judgmental service providers

- **Social**
  - Male partner approval
  - Parental approval
  - Community misconceptions and stigma

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**Zimbabwe**

The DPP pill is good, but if we look at it closely when its combined [PrEP and COC] .... the side effects will be many, they [the side effects] will be dual as well.

**South Africa**

The last time I went ... looking for PrEP ... they straight up denied giving [it] me and said no.

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Tenza, S. et al. (2021) “One Stone, Two Birds: Perspectives of health care providers (HCP) and women regarding the dual prevention pill (DPP) for pregnancy and HIV prevention in Johannesburg, South Africa,” Oral Abstract Presentation (virtual) at Adherence 2021, Nov 7-9 Orlando.


Source: focus group discussions with women ages 16–40 from South Africa and Zimbabwe (14 FGDs, 104 participants)
Market Size
• 250,000 to 1.25M women currently using COCs, condoms, or with an unmet need may use the DPP
• Potentially a 2- to 10-fold increase in PrEP usage

Cost-Effectiveness
• Likely to be cost-effective in settings with higher HIV burden and low ART coverage
• More cost-effective than oral PrEP if adherence enhanced
• Likely cost-saving among FSWs, sero-discordant couples

doi: [10.1136/bmjsh-2020-200662](https://doi.org/10.1136/bmjsh-2020-200662)

Malali, et al. (2022) Understanding Cost-Effectiveness of the Dual Prevention Pill. Presentation to the DPP Advisory Board.
Will PrEP adherence be enhanced with the DPP?

Will people prefer to use and continue using the DPP compared to oral PrEP?
HPTN 104

Adherence to a dual prevention pill (TDF/FTC + a combined oral contraceptive) versus a two pill regimen
Primary Objective

Compare adherence to the DPP versus two pill regimen
Secondary Objectives

Preference
Adherenece *during Choice*
Persistence *during Choice*
Tolerability, Side Effects
Acceptability
Exploratory Objective

Examine *facilitators and barriers* of DPP adherence, acceptability, and persistence
HPTN 104 Overview

- Open-label, multisite, randomized, crossover trial: DPP versus 2 pill regimen (2PR)
- N= 1,000 people of childbearing potential ages 16-35 years old
  - 800 people of childbearing potential ages 18-35
  - 200 adolescents

<table>
<thead>
<tr>
<th>Screening</th>
<th>Enrollment Randomization (1:1)</th>
<th>RANDOMIZED CROSS OVER PERIOD</th>
<th>CHOICE PERIOD</th>
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<td>N</td>
<td>Period 1 (12 Weeks)</td>
<td>Period 2 (12 Weeks)</td>
<td>Period 3 (24 Weeks)</td>
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<tr>
<td>Arm 1 500</td>
<td>DPP</td>
<td>2PR</td>
<td>Free choice (DPP or 2PR or neither)</td>
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<tr>
<td>Arm 2 500</td>
<td>2PR</td>
<td>DPP</td>
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Qualitative sub-study: In-depth interviews with up to 100 participants
Timeline

- **HPTN SRC Submission**: May 2022
- **DAIDS Review Site Selection**: July–Aug. 2022
- **Develop and pilot instruments/counseling materials**: Q3 2022-Q1 2023
- **Study Close out**: Mid 2025

**June/July 2022**
- SRC Revisions
- DAIDS and Viatris Submission

**Sept/Oct 2022**
- Site IRB/EC/Reg submission

**Mid 2023**
- Study Launch
Protocol Team

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Population Council

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• The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.