# Antiretroviral Pre-Exposure Prophylaxis for HIV-1 Prevention among Heterosexual African Men and Women: The Partners PrEP Study

Jared Baeten, MD PhD & Connie Celum, MD MPH
on behalf of
The Partners PrEP Study Team


Study Funder: Bill & Melinda Gates Foundation

# Partners PrEP Study

**4758 HIV discordant couples**

↓

**Randomize HIV- partners**
**(normal liver, renal, hematologic function; not pregnant/breastfeeding)**

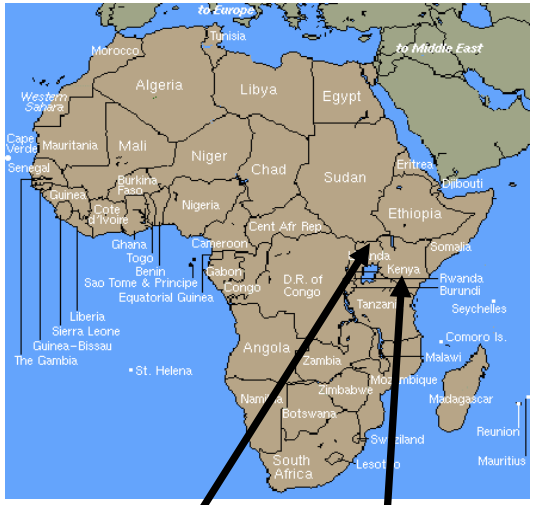
↙ ↓ ↘

TDF once daily | FTC/TDF once daily | Placebo once daily

**All receiving HIV** ↓ **prevention services**

Follow couples for 24-36 months

**1° endpoint: HIV infection in HIV-negative partner**
**Co- 1° endpoint: Safety**




Jinja, Kabwohe, Kampala, Mbale, Tororo, **Uganda**

Eldoret, Kisumu, Nairobi, Thika, **Kenya**

PARTNERS PrEP STUDY

# Study Procedures

**HIV- participants**

- Monthly HIV & pregnancy testing
- Monthly symptom & 3-monthly laboratory safety monitoring
- Monthly provision of study medication and individualized adherence counseling, including not sharing study drug

**HIV+ participants**

- 3-monthly visits
- 6-monthly CD4 counts
- ongoing HIV primary care
- active referral for ART following national guidelines

***All participants: comprehensive HIV prevention package***

- *Risk reduction counseling (individual and couple)*
- *Free condoms and condom counseling*
- *Contraception counseling and provision*
- *Screening and treatment for STIs*
- *Counseling & referral for other HIV prevention interventions (e.g., male circumcision), per national policies*

# Population characteristics

| | Total (n=4747*) | TDF (n=1584) | FTC/TDF (n=1579) | Placebo (n=1584) |
|---|---|---|---|---|
| **HIV- partner female / male** | 38% / 62% | 38% / 62% | 36% / 64% | 39% / 61% |
| **Age of HIV- partner**, years (median/IQR) | 33 (28,40) | 33 (28,40) | 33 (28,40) | 33 (28,40) |
| **Couple married** | 98% | 97% | 98% | 98% |
| **Duration of partnership**, years (median/IQR) | 7 (3,14) | 7 (3,14) | 7 (3,14) | 7 (3,14) |
| **Duration known HIV serodiscordant**, years (median/IQR) | 0.4 (0.1,2.0) | 0.5 (0.1,2.0) | 0.4 (0.1,2.0) | 0.4 (0.1,2.0) |
| **CD4 count, HIV+ partner,** cells/$mm^3$ (median/IQR) | 495 (375,662) | 491 (370,661) | 497 (380,664) | 499 (375,663) |
| **Plasma viral load, HIV+ partner,** $log_{10}$ copies/mL (median/IQR) | 3.9 (3.2, 4.5) | 3.9 (3.2,4.5) | 3.9 (3.1,4.5) | 3.9 (3.2,4.5) |
| **Started ART, HIV+ partner,** during follow-up | 19% | 20% | 18% | 20% |



* 11 couples found after randomization to be ineligible and exited from the study

# Retention & Adherence

- 95% retention

- Primary measure of adherence = monthly pill count of unused study product

| | Total | TDF | FTC/TDF | Placebo |
|---|---|---|---|---|
| **Dispensed doses taken** | 97% | 97% | 97% | 97% |
| **Pill bottles returned** | 98% | 98% | 98% | 98% |

# Primary efficacy results

Primary analysis: modified intention-to-treat (mITT) of 78 events (as of May 31, 2011)

- Excluding infections present at randomization (3 TDF, 3 FTC/TDF, 6 placebo)

| | TDF | FTC/TDF | Placebo |
|---|---|---|---|
| **Number of HIV infections** | 18 | 13 | 47 |
| **HIV incidence,** per 100 person-years | 0.74 | 0.53 | 1.92 |
| **HIV protection efficacy, vs placebo** | **62%** | **73%** | |
| 95% CI | (34-78%) | (49-85%) | |
| p-value | 0.0003 | <0.0001 | |
| Z-score, vs. $H_0$=0.7 | -2.17 | -2.99 | |

***Effect of TDF and FTC/TDF statistically similar (p=0.18)***

ITT analysis results similar

# Safety

- No statistically significant difference in deaths, SAEs, key laboratory AEs

| *Number of participants with each safety event* | **Total** | **TDF** | **FTC/TDF** | **Placebo** |
|---|---|---|---|---|
| **Death*** | 24 (<1%) | 8 | 7 | 9 |
| **SAE**** | 320 (7%) | 108 | 107 | 105 |
| **Confirmed creatinine AE** | 49 (1%) | 17 | 20 | 12 |
| **Confirmed phosphorus AE** | 403 (9%) | 138 | 133 | 132 |

* No deaths related to study products

** Primarily lab events; clinical events reflect population morbidity (e.g., malaria & trauma)

# Tolerability

- Monthly 19-item symptom questionnaire

| *% of participants reporting symptom* | **TDF** | **FTC/TDF** | **Placebo** | **P-value TDF vs. Placebo** | **P-value FTC/TDF vs. Placebo** |
|---|---|---|---|---|---|
| **Nausea** | | | | | |
| All visits | 1.6% | 1.7% | 1.5% | p=0.23 | p=0.18 |
| Month 1 | 6.3% | 5.9% | 4.5% | p=0.03 | p=0.07 |
| **Diarrhea** | | | | | |
| All visits | 1.6% | 1.8% | 1.4% | p=0.18 | p=0.02 |
| Month 1 | 4.1% | 4.5% | 2.8% | p=0.06 | p=0.02 |

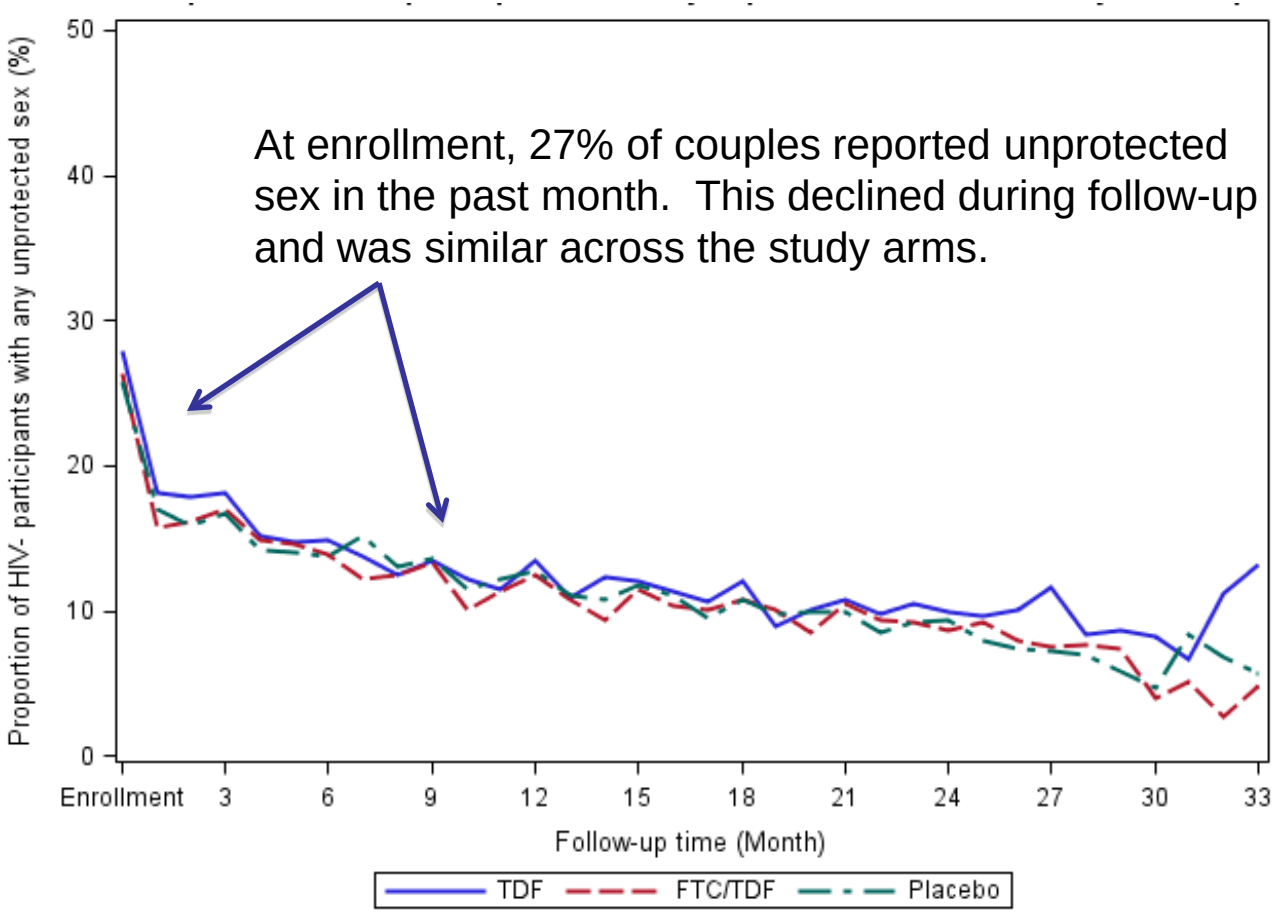
# Pregnancy

- Among HIV- women (n=1785):

| | Total | TDF | FTC/TDF | Placebo |
|---|---|---|---|---|
| **Number of pregnancies** | 272 | 107 | 76 | 89 |
| **Pregnancy incidence,** per 100 woman-years | 10.3 | 12.1 | 8.9 | 9.9 |
| ***P-value vs. placebo*** | | *p=0.12* | *p=0.50* | |
| **Time off study drug due to pregnancy** | 1.8% | 2.6% | 1.4% | 1.6% |

Hormonal contraceptive use at most recent study visit:
10% OCP, 26% injectable, 8% implant

# Sexual behavior




-From prior studies of serodiscordant couples (HPTN 052 & Partners in Prevention HSV/HIV Transmission Study), ~30% of infections acquired from 'outside' partner

# Ongoing testing

- Testing ongoing for the following, not yet available:
  - HIV resistance in seroconverters
  - HIV plasma viral load in seroconverters
  - Plasma / intracellular drug levels in seroconverters and subset of non-seroconverters

# Partners PrEP Summary

- **TDF and FTC/TDF PrEP reduced risk of HIV acquisition by 62% & 73% in African men & women**
  - Results announced July 2011, based on interim DSMB review of data through May 31, 2011
- **TDF and FTC/TDF PrEP were safe & well-tolerated**
- **No evidence of risk compensation**
- **Partners PrEP Study is continuing, based on DSMB recommendations to:**
  - Gather comparative information on efficacy, safety, tolerability and resistance with TDF vs. FTC/TDF PrEP
  - Offer placebo arm participants active PrEP

# Proposed Demonstration Projects

Among newly-identified HIV serodiscordant couples in East Africa, assess delivery, uptake of, & adherence to open label PrEP, including:

1) Feasibility of targeting and uptake of PrEP

2) Monthly versus quarterly HIV-1 testing

3) Adherence to open label PrEP in a "real world" context

4) Risk perception, sexual risk behavior, & fertility

5)Pregnancy outcomes among females on PrEP who become pregnant (through a separate linked protocol)

# Partners PrEP Study Team

- **University of Washington Coordinating Center**
  **Connie Celum (PI), Jared Baeten (Co-Chair and Medical Director), Deborah Donnell (Statistician), Justin Brantley, Tami Cloutier, Robert Coombs, Amy Dao, Shauna Durbin, Mira Emmanuel-Ogier, Lisa Frenkel, Carlos Flores, Harald Haugen, Renee Heffron, Ting Hong, Jim Hughes, Erin Kahle, Johanna Karas, Becky Karschney, Lara Kidoguchi, Meighan Krows, Matt Leidholm, Jai Lingappa, Toni Maddox, Angela McKay, Julie McElrath, Allison Mobley, Susan Morrison, Nelly Mugo, Andrew Mujugira, Vikram Nayani, Patrick Ndase, Apollo Odika, Hilda O'Hara, Dana Panteleeff, Jennifer Revall, Marothodi Semenya, John Sparkman, Kathy Thomas, Ellen Wilcox**
- **Sites**
  - **Eldoret, Kenya (Moi U, Indiana U): Edwin Were (PI), Ken Fife (PI), Cosmas Apaka**
  - **Jinja, Uganda (Makarere U, UW); Patrick Ndase (PI), Elly Katabira (PI), Fridah Gabona**
  - **Kabwohe, Uganda (KCRC): Elioda Tumwesigye (PI), Rogers Twesigye**
  - **Kampala, Uganda (Makarere U): Elly Katabira (PI), Allan Ronald (PI), Edith Nakku-Joloba**
  - **Kisumu, Kenya (KEMRI, UCSF): Elizabeth Bukusi (PI), Craig Cohen (PI), Josephine Odoyo**
  - **Mbale, Uganda (TASO, CDC): Jonathan Wangisi (PI), Jim Campbell (PI), Jordan Tappero (PI), Akasiima Mucunguzi**
  - **Nairobi, Kenya (KNH/U Nairobi, UW): James Kiarie (PI), Carey Farquhar (PI), Grace John-Stewart (PI), Harrison Tamooh, Freda Kinoti**
  - **Thika, Kenya (KNH/U Nairobi, UW): Nelly Mugo (PI), Kenneth Ngure**
  - **Tororo, Uganda (CDC, TASO): Jim Campbell (PI), Jonathan Wangisi (PI), Jordan Tappero (PI), Aloysious Kakia**
- **DF/Net** (data center)**: Lisa Ondrejcek, Darryl Pahl, Jae Chong**
- **CLS** (laboratory oversight)**: Wendy Stevens, Charlotte Ingram, Ute Jentsch, Mukthar Kader, Nombulelo Gqomane, Feroza Bulbulia, Jan van den Heuvel**
- **ClinPhone/Perceptive Informatics** (randomization)
- **Gilead** (study drug)**: Jim Rooney, Raj Sangha, Abboud Habr, Farideh Said**
- **Bill & Melinda Gates Foundation** (study funder)**: Stephen Becker**
- **HIV serodiscordant couples who test, screen, & participate**

PARTNERS PrEP STUDY