2nd Long-Acting Treatment and Prevention Conference

29 October 2024 | Johannesburg

Long-acting PrEP in Pregnancy & Breastfeeding

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Background:
High HIV incidence during pregnancy & breastfeeding

AIDS (London, England)
Author Manuscript HHS Public Access

Incident HIV among pregnant and breastfeeding women in sub-Saharan Africa: a systematic review and meta-analysis

Lauren A. GRAYBILL, Margaret KASARO, [...], and Benjamin H. CHI

- Meta analysis of 37 studies:
- Estimated average HIV incidence rate in pregnant and breastfeeding women was 3.6 per 100 women years (95% PI: 1.2, 11.1)
- HIV incidence was associated with age, partner HIV status, and calendar time

Variable	Stratum-specific estimates			
	Number of estimates	Pooled incidence rate	(95% PI)	
Reproductive periods observed during study follow-up				
Pregnancy only	11	4.3	(1.4–13.0)	1.0
Breast-feeding only	5	3.8	(1.2–11.9)	0.9
Pregnancy and breast-feeding	10	3.8	(1.2–11.6)	0.9
Pregnancy, breast-feeding, nonpregnant/non-breast-feeding	8	2.7	(0.9–8.3)	0.6

Why is HIV risk elevated in pregnancy & breastfeeding?

BIOLOGICAL FACTORS

HORMONAL CHANGES
Increased **estrogen & progesterone**

- Genital tract **expression of cell receptors** targeted by HIV (CCR5 and CXCR4)

PREGNANCY-INDUCED IMMUNE ADAPTATIONS

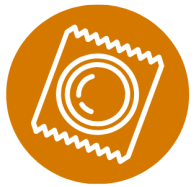
- **Activated innate immunity** (increased inflammation and HIV target cells in genital tract)
- **Suppressed adaptive immunity** (reduced NK cells)
- **Alterations in vaginal microbiome**

STIS
High **prevalence & incidence** (incl. BV)

POSTPARTUM
Trauma (micro and macro) caused by vaginal delivery and vaginal dryness

BREASTFEEDING
Low levels of **estrogen**

SOCIO-BEHAVIORAL FACTORS



CONDOM USE
Condomless sex before, during and after pregnancy

SEXUAL NETWORK
>1 sex partner, or partner has **other partners**

IPV
Intimate partner **violence**, incl. sexual violence

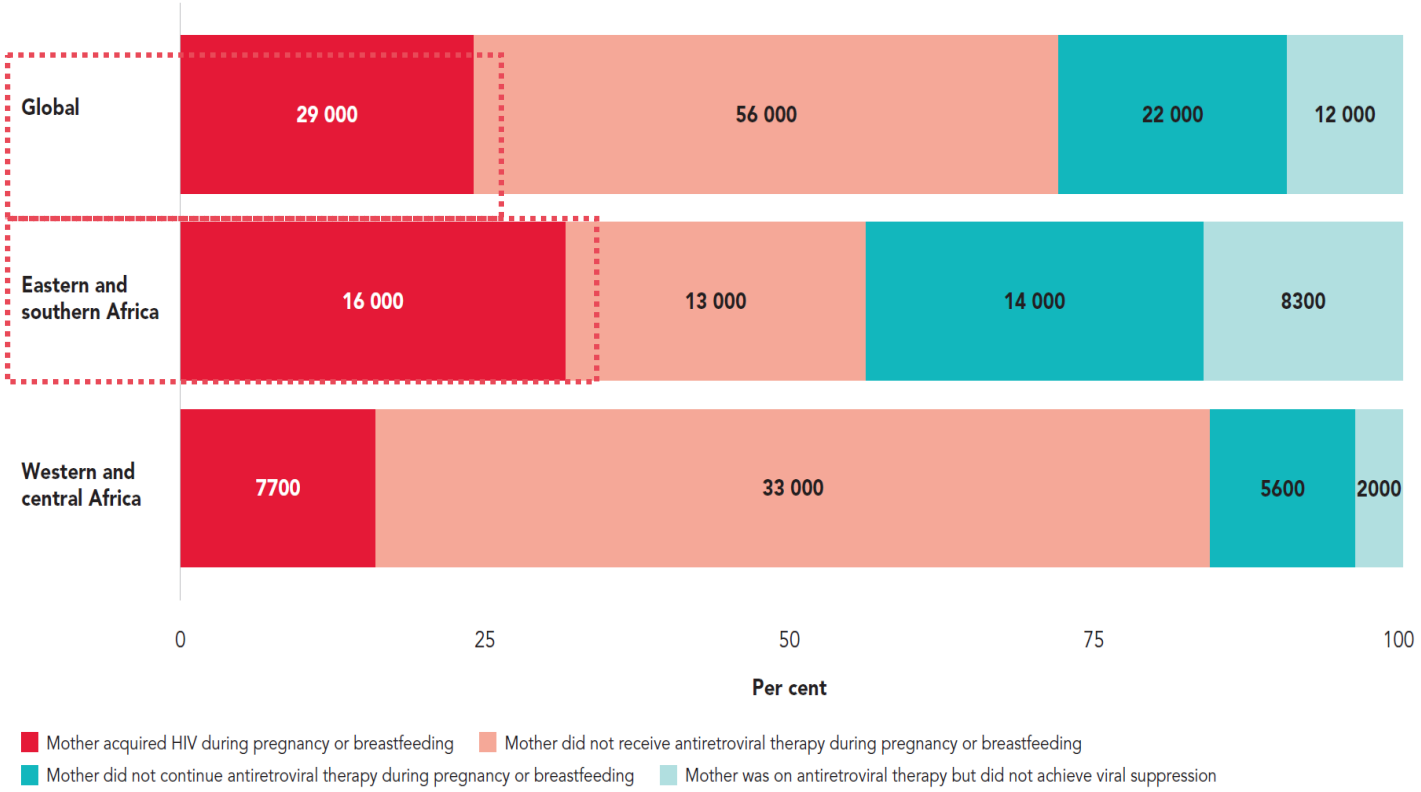
STIGMA
HIV-related stigma leading to **decreased HIV testing/ PrEP use**

SUBSTANCE USE
Increased risk of **HIV exposure** due to impact on sexual behavior

Sources: Thomson et al,2018; Joseph Davey et al. 2018

One in four infant infections due to HIV acquisition in pregnancy and breastfeeding

Figure 4.3 Percentage of new vertical HIV infections by cause of transmission, global and selected regions, 2023



- **Global: 1/4 infant infections** attributed to incident maternal HIV
- **East and Southern Africa: 1/3 infant infections** attributed to incident maternal HIV
  - 29,000 infant HIV infections from incident HIV during pregnancy or breastfeeding
  - 16,000 infant infections in E. And Southern Africa (55% of global cases)

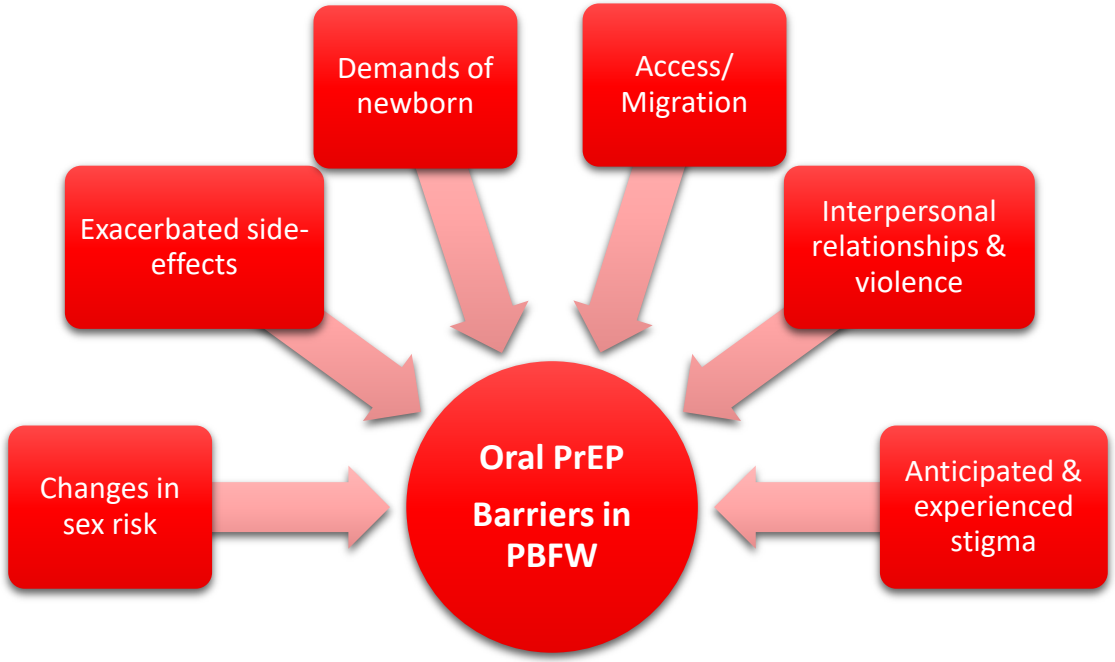
Causes of vertical transmission of HIV

Source: 2024 global AIDS report — The Urgency of Now: AIDS at a Crossroads | UNAIDS

Building on prior studies of oral PrEP in pregnancy and breastfeeding women

PrEP-PP
Pre-exposure Prophylaxis in Pregnancy & Postpartum

- Cohort of 1300 pregnant and postpartum women in Cape Town (2018-2022)
- 84% started oral PrEP at first ANC visit
- Persistence dropped to 50% by 6 months (in postpartum) and 32% at 12 months
- HIV incidence high in women who stopped using PrEP in postpartum
- Important barriers that could be mitigated with LA-PrEP



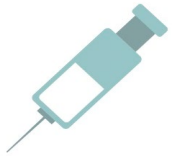
Joseph Davey et al. PrEP-PP, Lancet HIV, JIAS 2023, 2024

Importance of PrEP continuation: HIV seroconversion in postpartum period

- **Most seroconversion in postpartum period:**
  - 1 pregnant and 15 postpartum people seroconverted
  - 2 infants HIV+ (12.5% in seroconverters)
    - 1 in labor/delivery and 1 following breastfeeding

- **PrEP use in seroconverters: <u>Mostly due to discontinued PrEP use in postpartum period :</u>**
  - **10 people started PrEP but discontinued** (66%) >6 months prior to seroconversion
  - **4 people took PrEP intermittently or stopped >30 days** prior to seroconversion
  - **2 people never started PrEP** (13%)

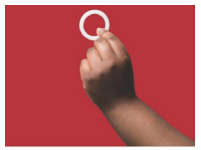
New PrEP modalities and differentiated delivery to reduce barriers to oral PrEP



Injectable cabotegravir (CAB-LA): IM injection every 8 weeks

PURPOSE
Prevention with PURPOSE

Lenacapavir injection (**LEN**): subcutaneous injection every 6 months (investigational product)



Dapivirine ring: inserted into the vagina every 4 weeks

Differentiated PrEP delivery: multi-month dispensing, pharmacy or community, rapid queue, use of HIV self-testing for PrEP pick-up

Sources: Baeten, J. et al, *The Lancet. HIV* (2021); Delany-Moretlwe, et al, *Lancet* (2022); World Health Organization. (2022); Bekker, LG. et al, New England Journal of Medicine (2024)

Potential benefits of CAB-LA: Model from South Africa

- **Without PrEP: 1.31 million new HIV infections (2025-2035) in South Africa including:**
  - 100,000 in pregnant & breastfeeding people
  - 16,800 in infants at/before birth
  - 35,200 in infants through breastmilk
- **Model used three scenarios:**
  1. Oral PrEP only
  2. CAB-LA only
  3. Oral PrEP and CAB-LA choice

- **Model informed by South African data** on CAB-LA and oral PrEP in pregnancy
- **HIV incidence reductions in pregnant & breastfeeding women (PBW) & infants:**
  1. **Oral PrEP only:** 8.6% PBW & 9.3% reduction infants
  2. **CAB-LA only**: 41% PBW & 43% reduction in infants
  3. **Choice between oral and CAB:** 39%PBW & 40% in infants

AIDS. 2024 Mar 15;38(4):589-594. doi: 10.1097/QAD.0000000000003803. Epub 2023 Dec 4.

The potential benefits of long-acting injectable cabotegravir in pregnant and breastfeeding women and their infants

Leigh F Johnson [1], Landon Myer [2], Lise Jamieson [3 4 5], Gesine Meyer-Rath [3 5 6], Sinead Delany-Moretlwe [7], Dvora Joseph Davey [2 8]

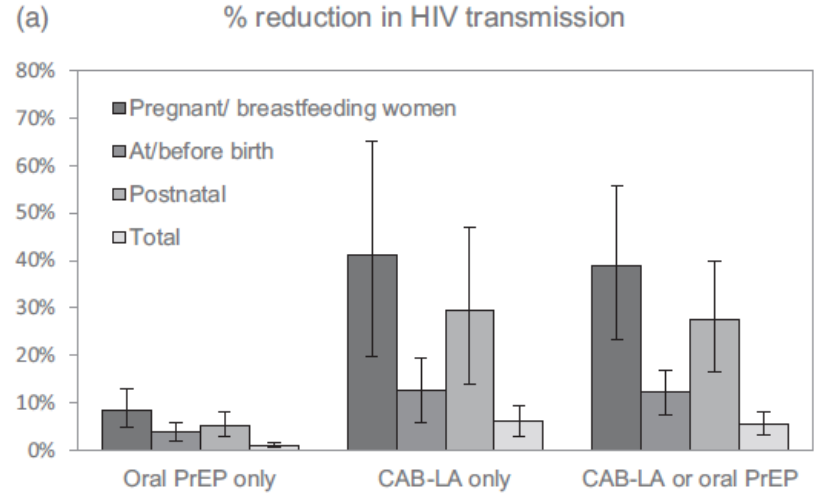


Fig. 1. Impact and efficiency of promoting preexposure prophylaxis to pregnant and breastfeeding women. Bars represent the average from 1000 simulations; error bars represent the 2.5th and 97.5th percentiles of the model

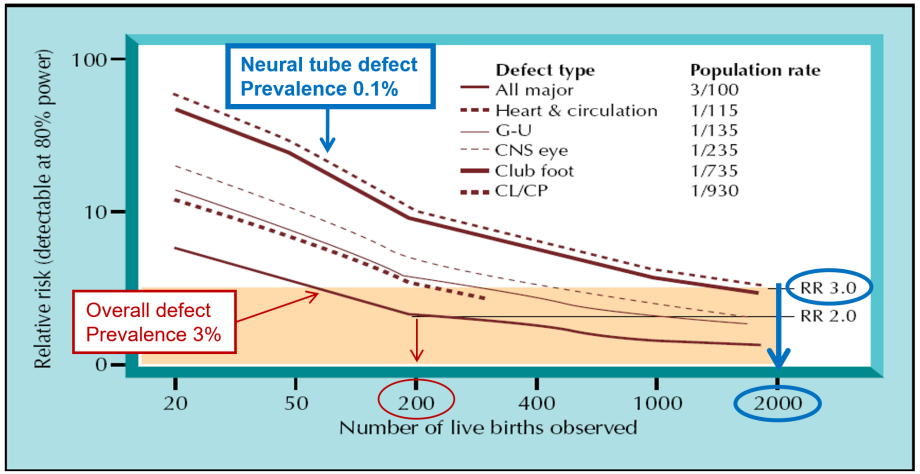
Injectable PrEP appears safe in pregnancy: Data from HPTN-084 (and OLE) & PURPOSE 1

- **CAB-LA:** Data on safety in **288 pregnancies with CAB-LA PrEP exposure at conception**, 212 continued CAB in pregnancy (351 pregnancies including OLE) (Delany-Moretlwe, et al, IAS 2024)
- CAB-LA dosing in pregnancy appears appropriate (Marzinke, et al. IAS, 2024)
- **Pregnancy outcomes with CAB-LA at conception similar to background rates** & in those with no CAB exposure.
- **LEN:** Data on safety in **105 completed pregnancy with LEN exposure at conception** (Bekker, NEJM, 2024)
- **No significant differences in pregnancy outcome between LEN vs oral PrEP.**
- **Both drugs indicate safety to mother and fetus.**

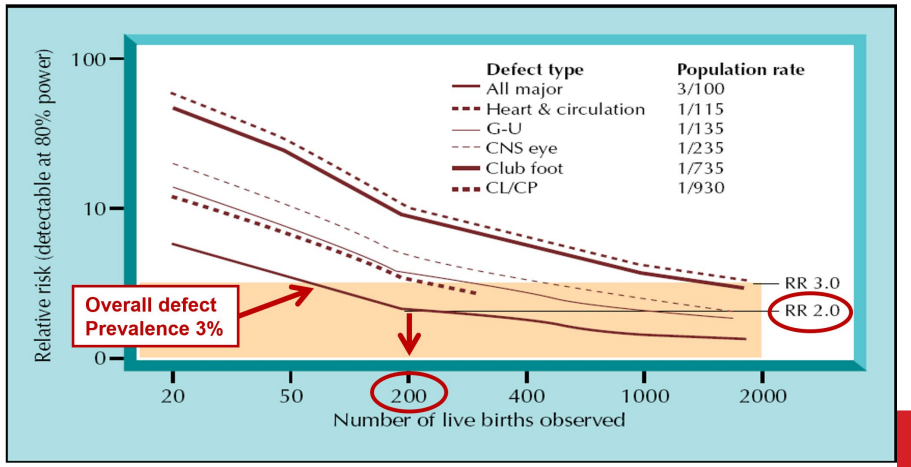
Well done to the HPTN 084 and PURPOSE teams for getting this data – and to PURPOSE for building this into trial!

Data collection on safety in pregnancy continues for CAB-LA or LEN

- **For CAB-LA PrEP and LEN:** with between 200-300 births with exposure at conception:
  - Can rule out 1.5-fold increase in risk of outcomes with background rate >10% (miscarriage, pre-term delivery).
  - Can rule out ~2-fold or more increase in outcomes with background rate ~3% (stillbirth, overall birth defects).
  - For outcomes with background rate <3% (specific birth defects, neonatal mortality), **insufficient data to determine if even a 3-fold increase in risk**.
  - **WHO ongoing data collection from partners with CAB-LA exposed pregnancies**



Watts DH. Curr HIV/AIDS Rep 2007;4:135-140



Watts DH. Curr HIV/AIDS Rep 2007;4:135-140

Discrete choice experiment in pregnant and postpartum women (E. London, Cape Town & Gaborone, n=450)

TYPES OF LONG-ACTING PrEP (PRE-EXPOSURE PROPHYLAXIS):

	INJECTABLE PREP	VAGINAL RINGS	LONG-ACTING PILL	ARM IMPLANT
HOW EFFECTIVE IS IT AT PREVENTING HIV?	HIV risk reduced by **89%** in women ages 18-45	HIV risk reduced by **30%** in women ages 18-45	**Currently being studied** in humans	**Currently being studied** in humans
HOW TO USE:	Intramuscular injection in buttock	Small flexible ring inserted into vagina	Taken orally	Inserted in arm just under skin
HOW OFTEN:	Every 8 weeks	Replace every 30 days	Once per month	Once per year

Because if I go there [to the clinic] frequently people will start noticing that I take pills but if I go once no one will know. (Cape Town, pregnant, PrEP experienced)

This pill I might forget at times… and this arm implant I'm also scared but as for injection it's just here and there. (Botswana, breastfeeding, PrEP Naïve)

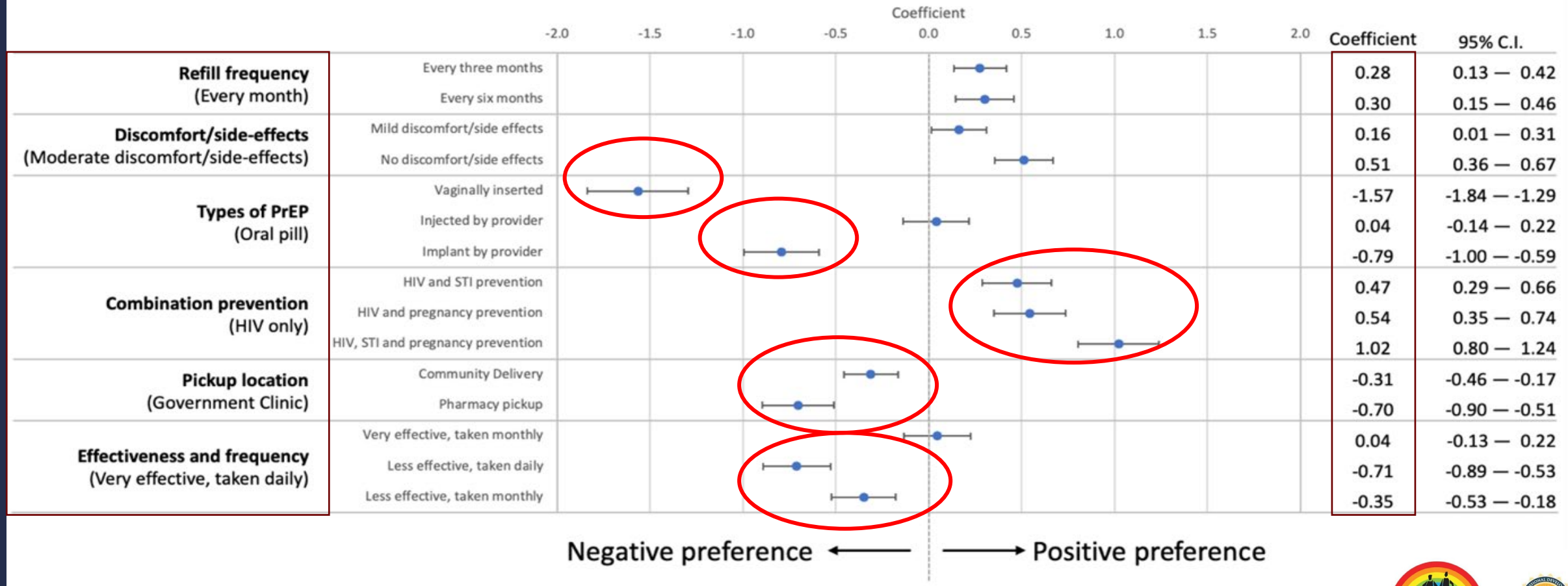
I am disappointed because I thought it (vaginal ring) prevents all the infections. (Cape Town, pregnant, PrEP experienced)

That we have one thing for multiple situations (MPTs). It will be difficult for me to go for my contraceptives this week, next week I go for something else. (East London, pregnant, PrEP naïve)

I want it to last for a long time. It should not have side effects when they insert it or have an infection… I need to know how it reacts… (East London, breastfeeding, PrEP naive)

I'm really against being touched around the vagina every month so I just can't. I would choose the pill, because with it it's easy. It's just to drink it right? (Gaborone, breastfeeding, PrEP naïve)

Pregnant and bf women prefer fewer refills, combination prevention & injectional PrEP



		Coefficient	95% C.I.
Refill frequency (Every month)	Every three months	0.28	0.13 — 0.42
	Every six months	0.30	0.15 — 0.46
Discomfort/side-effects (Moderate discomfort/side-effects)	Mild discomfort/side effects	0.16	0.01 — 0.31
	No discomfort/side effects	0.51	0.36 — 0.67
Types of PrEP (Oral pill)	Vaginally inserted	-1.57	-1.84 — -1.29
	Injected by provider	0.04	-0.14 — 0.22
	Implant by provider	-0.79	-1.00 — -0.59
Combination prevention (HIV only)	HIV and STI prevention	0.47	0.29 — 0.66
	HIV and pregnancy prevention	0.54	0.35 — 0.74
	HIV, STI and pregnancy prevention	1.02	0.80 — 1.24
Pickup location (Government Clinic)	Community Delivery	-0.31	-0.46 — -0.17
	Pharmacy pickup	-0.70	-0.90 — -0.51
Effectiveness and frequency (Very effective, taken daily)	Very effective, taken monthly	0.04	-0.13 — 0.22
	Less effective, taken daily	-0.71	-0.89 — -0.53
	Less effective, taken monthly	-0.35	-0.53 — -0.18

Need for informed CHOICE in PrEP in pregnant and breastfeeding women

1) **PrEP-PP**: n=190 oral PrEP using PBFW in sub-study
2) **PrIMA-X**: RCT offering daily oral PrEP to PBFW in W. Kenya (n=204 in sub-study)

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY Open Access

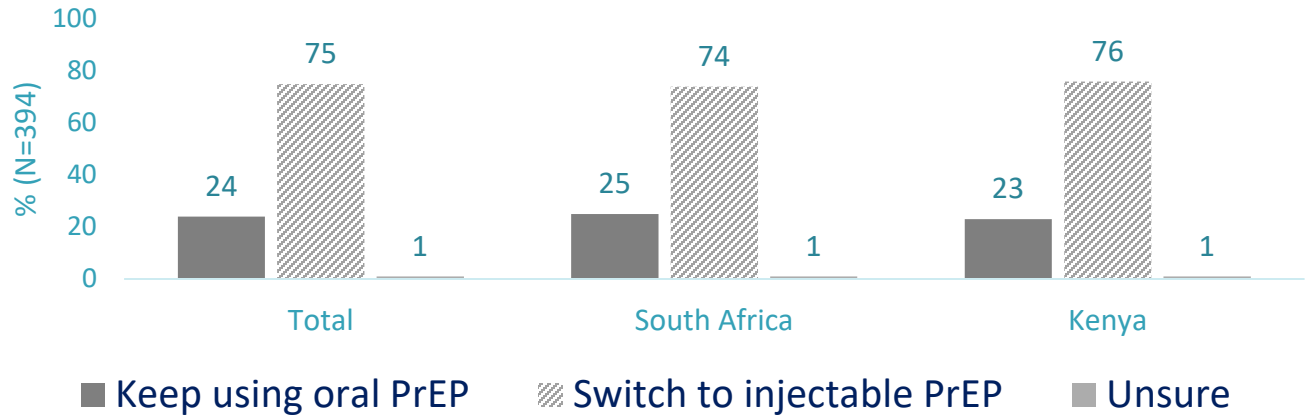
RESEARCH ARTICLE | Open Access

Preferences and acceptability for long-acting PrEP agents among pregnant and postpartum women with experience using daily oral PrEP in South Africa and Kenya

Nafisa J. Wara, Rufaro Mvududu, Mary M. Marwa, Laurén Gómez, Nyiko Mashele, Catherine Orrell, Corrina Moucheraud, John Kinuthia, Grace John-Stewart, Landon Myer, Risa Hoffman, Jillian Pintye, Dvora L. Joseph Davey

First published: 23 May 2023 | https://doi.org/10.1002/jia2.26088

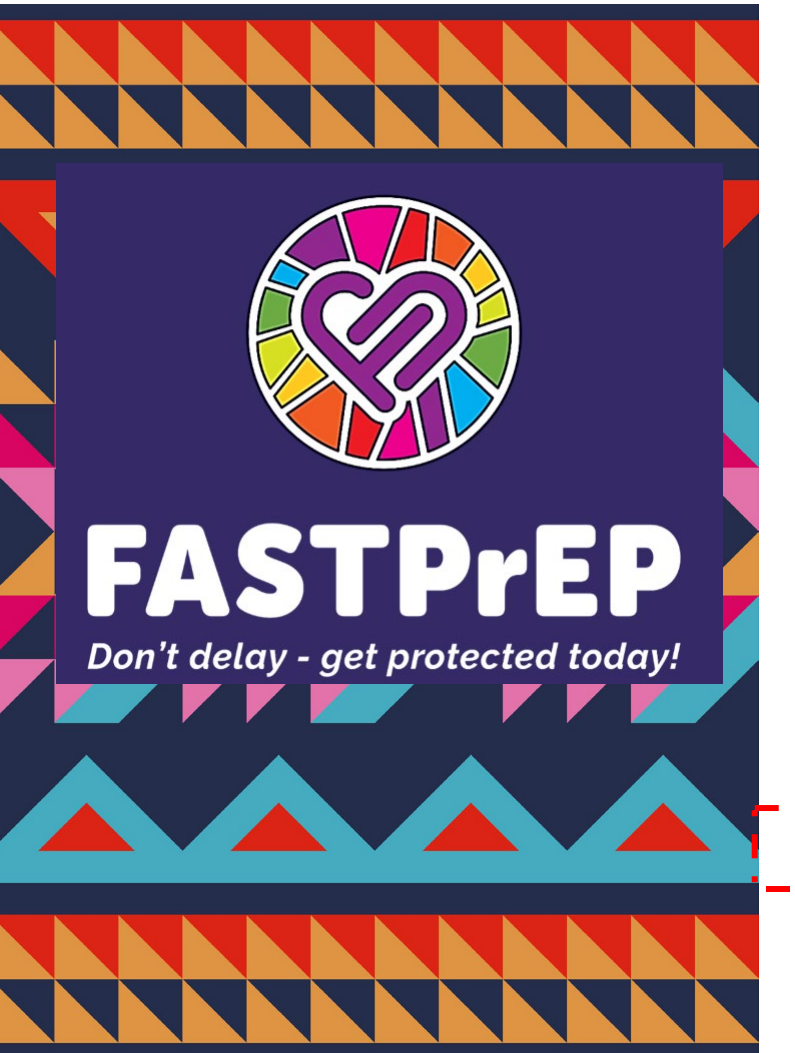
If injectable PrEP were approved as safe during pregnant or breastfeeding, would you prefer to keep using oral PrEP or switch to the injection?



75% of pregnant and postpartum people prefer injectable PrEP over oral PrEP

Source: Wara N, et al. JIAS June 2023; Participants were provided descriptions of injectable cabotegravir and dapivirine vaginal ring, including: method of insertion, effectiveness of HIV prevention, duration of effectiveness, described side effects

PrEPared to Choose: Ongoing implementation study in Cape Town



- Study enrolled young people (15-29 years) in a community-based mobile van and 1 clinic
- Offered oral PrEP or CAB-LA (vaginal rings not approved for PBFW at present) following choice counseling with option to switch modalities at follow-up visits over 18 months.
- Through Sept 2024:
  - 58 pregnant and breastfeeding people in study
  - 83% started CAB-LA
  - 27% started oral PrEP
- CAB-LA likes:
  - Ease of use and long-acting protection
  - Very likely to continue use (n=1 participant reported unlikely to continue due to injection pain)
  - 14% reported likely to use vaginal ring if approved for use in pregnancy and breastfeeding

Data collection ongoing through 2026 (incl persistence & birth outcomes)

Towards elimination of maternal HIV and HIV vertical transmission

Let's collaborate together to:

1. **Improve access to and counselling for effective PrEP use, incl injectable LA PrEP** in all pregnant & postpartum people who request or need it
2. ***Simplify* PrEP access by removing prescribing, lab and drug access barriers to improve continuation in pregnancy and postpartum**
   - Include differentiated, community delivery in postpartum
3. **Advocate for rapid, cost-effective CHOICE** including LEN, CAB-LA and DVR to improve effective use
4. **Improve health education and ongoing training in community and among healthcare providers** to encourage PrEP for PBFW and decrease stigma

Thank you to my dream team!

- Landon Myer, UCT
- Linda-Gail Bekker, DTHF/UCT
- Catherine Orrell, DTHF/UCT
- Tom Coates, UCLA
- Pamina Gorbach, UCLA
- Kate Dovel, UCLA
- Nafisa Wara, UCLA
- Rufaro Mvududu, UCT
- Sumaya Dadan, UCT
- Kalisha Bheemraj, UCT
- Sarah Schoetz Dean, UCLA
- South African National and W. Cape Provincial DOH
- **All pregnant & postpartum study participants**
- **Funder: National Institutes of Health (NICHD and NIMH)**

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