

# PrEP in Pregnancy and Breastfeeding: The Why, What and How

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Photo credit: Paul J. Brown Photography

# PrEP in Pregnancy and Breastfeeding: the Why, What, and How

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# Positionality

*\*I have no conflicts of interest to declare.*



# What do we know?

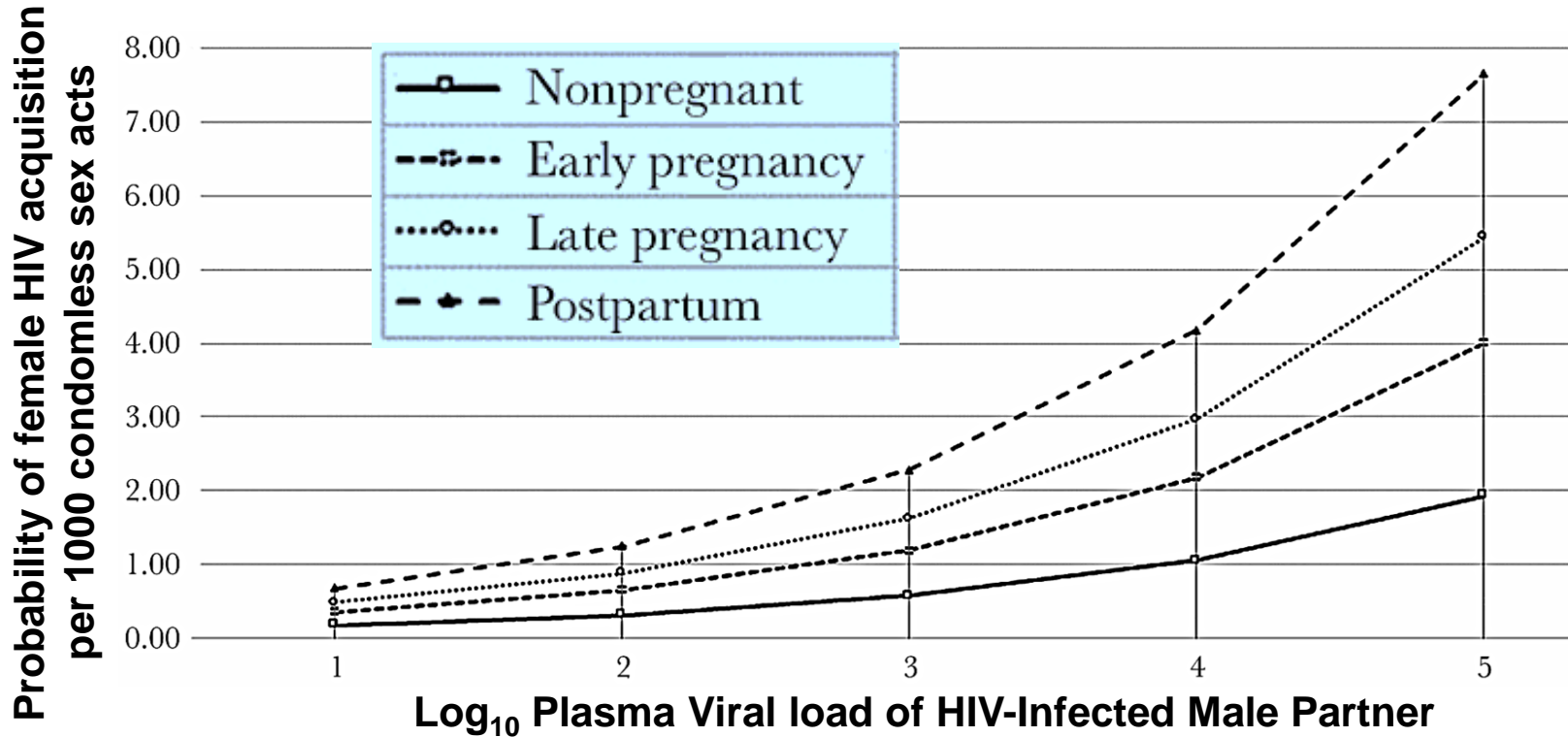
- ◆ PrEP appears safe in pregnancy
- ◆ WHO recommends PrEP in pregnancy
- ◆ Pregnant women want PrEP

# What don't we know?

- ◆ Longer-term infant outcomes
- ◆ Sustained PrEP use after birth
- ◆ Impact of novel PrEP agents



# Increased Per-Coital-Act risk of HIV Acquisition throughout Pregnancy and Postpartum



Thomson et al *JID* 2018





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POLICY BRIEF

# PREVENTING HIV DURING PREGNANCY AND BREASTFEEDING IN THE CONTEXT OF PREP

JULY 2017



MINISTRY OF HEALTH

## Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya

2016 Edition



# Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding

Lynne M. Mofenson<sup>a</sup>, Rachel C. Baggaley<sup>b</sup> and Ioannis Mameletzis<sup>b</sup>

- ◆ 33 studies, most among women living with HIV
- ◆ No association with pregnancy incidence, pregnancy loss, preterm delivery, low birth weight, small for gestational age, birth defects, or infant or maternal mortality

*“Given available safety data, there does not appear to be a safety-related rationale for prohibiting PrEP during pregnancy/lactation or for discontinuing PrEP...”*

Mofenson et al *AIDS* 2017





# PrEP safety studies among HIV-negative pregnant women

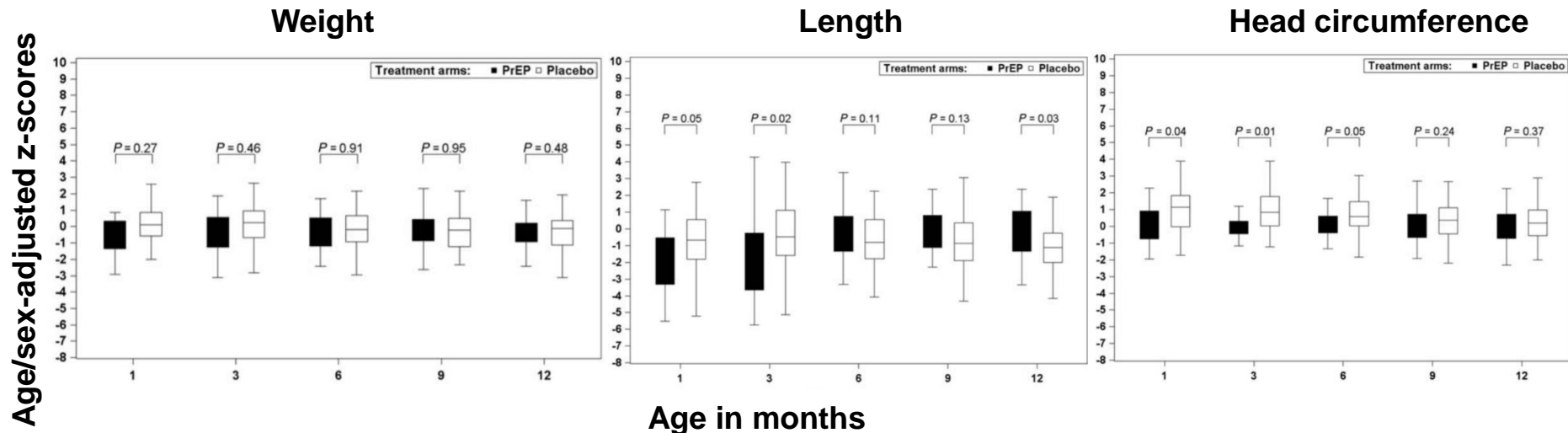
Study; Lead Author	PrEP-exposed pregnancies	Outcomes	
		Pregnancy	Infant
FEM-PrEP; Callahan 2015	n=69	No difference in outcomes by arm	None reported
Partners PrEP Study; Mugo 2014	n=335	No difference in pregnancy loss or preterm birth by arm	No difference in congenital anomalies, growth at 1-year
VOICE; Bunge 2015	n=263	No difference in pregnancy loss or preterm birth by arm	None reported
Partners Demo Project; Heffron 2018	n=30	No difference in pregnancy loss or preterm birth by PrEP use in pregnancy	PrEP-exposed infants lower z-score for length at 1-mo; no difference at 1-yr
PriYA Program; Dettinger 2018	n=246	No difference in preterm birth or birthweight by PrEP use in pregnancy	No difference in 6-week z-scores for length or weight





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# Partners Demonstration Project: Infant outcomes by PrEP exposure during pregnancy



- ◆ 30 women continued PrEP use in pregnancy in Demo; 96 pregnancies in placebo arm of Partners PrEP RCT
- ◆ PrEP-exposed infants had slightly lower z-scores at 1-month for length and head circumference; comparable at 1-year

Heffron et al *AIDS* 2018





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PrEP IMPLEMENTATION IN YOUNG  
WOMEN AND ADOLESCENTS

# Birth outcomes by PrEP exposure during pregnancy

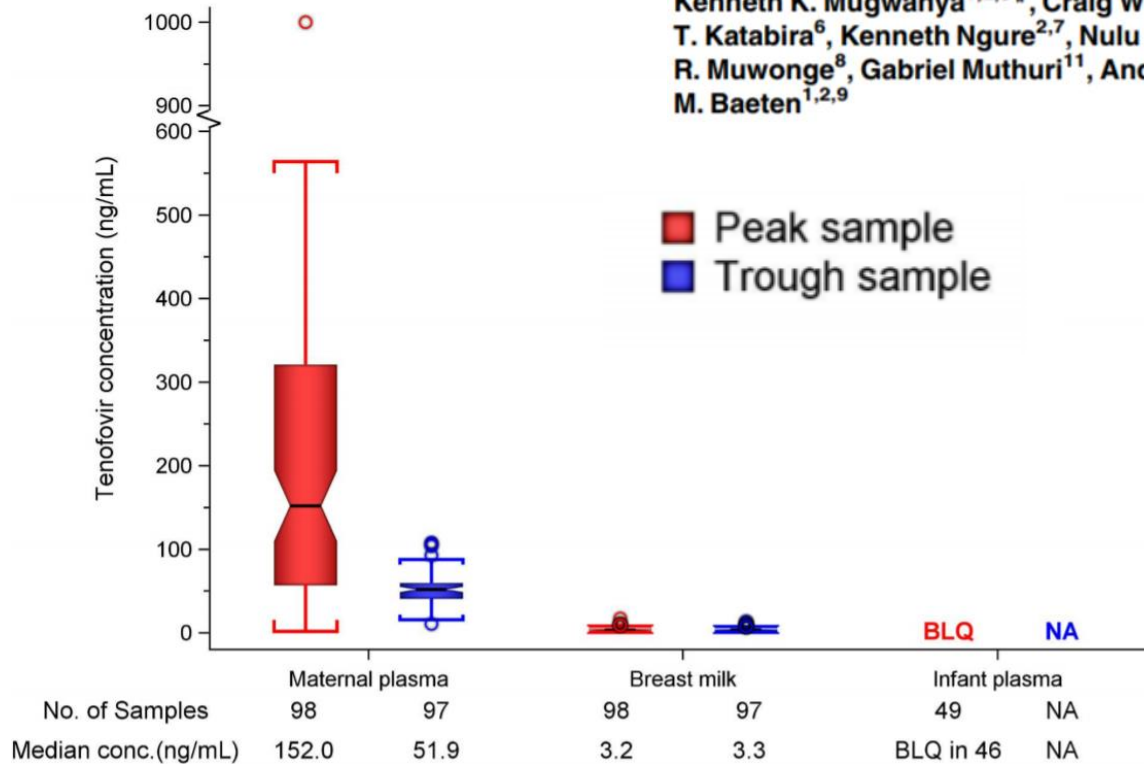
Birth outcome	PrEP exposed (n=246)	PrEP unexposed (n=7515)	p-value
Frequency of preterm birth	2.2%	3.5%	0.34
Median birth length (cm)	48	48	0.40
Median birth weight (kg)	3.4	3.3	0.01*
Congenital malformation	<1%	<1%	0.645

Dettinger et al *JIAS* 2019

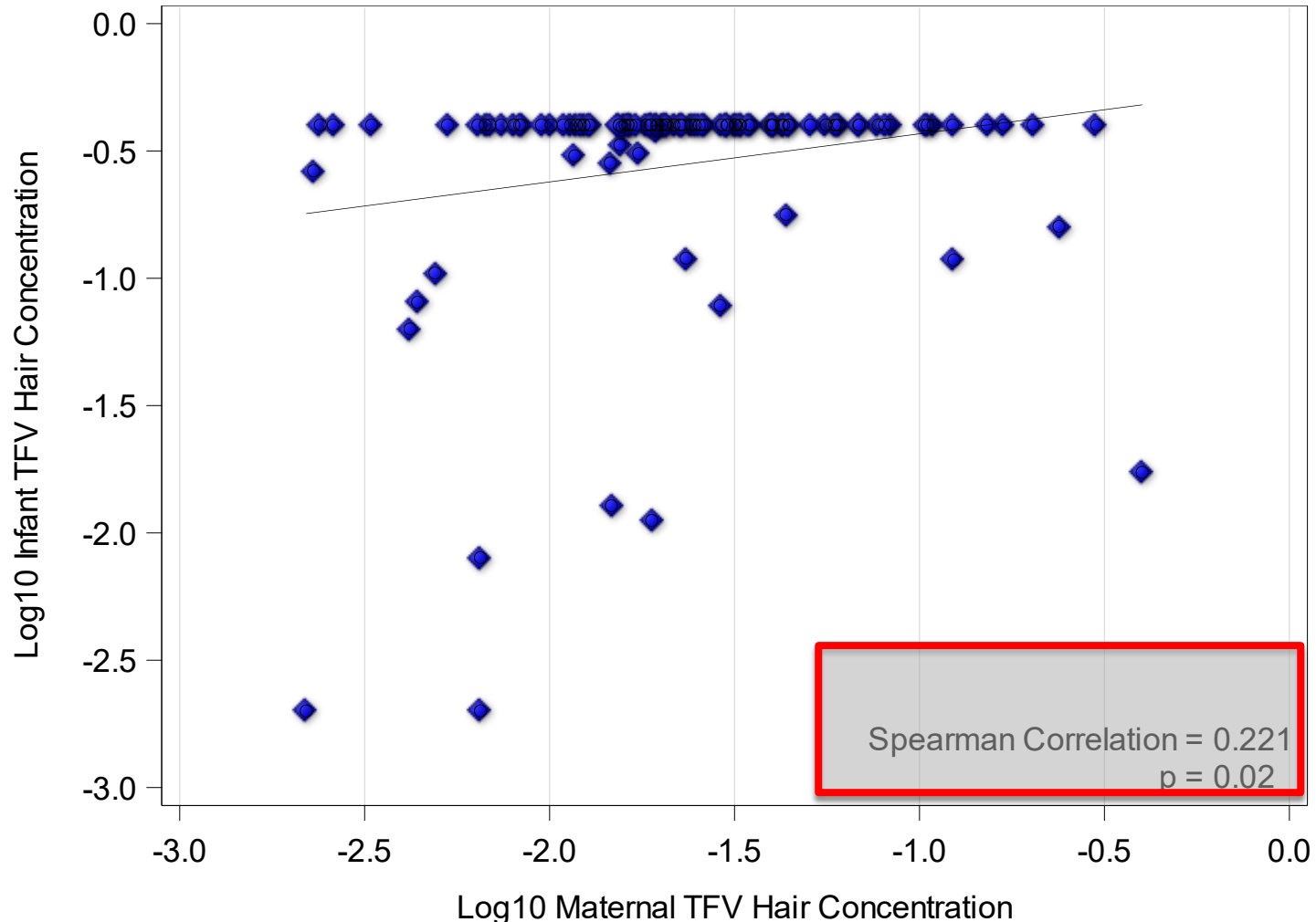


# Pre-exposure Prophylaxis Use by Breastfeeding HIV-Uninfected Women: A Prospective Short-Term Study of Antiretroviral Excretion in Breast Milk and Infant Absorption

Kenneth K. Mugwanya<sup>1,2,3\*</sup>, Craig W. Hendrix<sup>4</sup>, Nelly R. Mugo<sup>2,5</sup>, Mark Marzinke<sup>4</sup>, Elly T. Katabira<sup>6</sup>, Kenneth Ngunjiri<sup>2,7</sup>, Nulu B. Semiyaga<sup>8</sup>, Grace John-Stewart<sup>1,2,9,10</sup>, Timothy R. Muwonge<sup>8</sup>, Gabriel Muthuri<sup>11</sup>, Andy Stergachis<sup>2,12</sup>, Connie L. Celum<sup>1,2,9</sup>, Jared M. Baeten<sup>1,2,9</sup>



Mugwanya et al *PLOS Med* 2016

**Maternal by infant  $\text{Log}_{10}$  TFV hair concentration at birth (N=103)**

<sup>1</sup> For pregnancies (n=2) with infant hair level < LLOQ, the value LLOQ (=0.002 ng/mg) was used; for pregnancies with hair level > ULOQ (1 maternal hair; 82 infant hair), the value ULOQ (=0.4 ng/mg) was used



## Maternal and infant TFV hair concentrations (n=103) <sup>1</sup>

	Mean (SD)	Median (IQR)	Min, Max
<b>Maternal</b>			
Weight-normalized TFV hair concentration (ng/mg)	0.04 (0.06)	0.02 (0.01, 0.04)	0.002, 0.40
Log <sub>10</sub> weight-normalized TFV hair concentration	-1.64 (0.46)	-1.68 (-1.91, -1.37)	-2.66, -0.40
<b>Infant</b>			
Weight-normalized TFV hair concentration (ng/mg)	0.35 (0.12)	0.40 (0.40, 0.40)	0.002, 0.40
Log <sub>10</sub> weight-normalized TFV hair concentration	-0.55 (0.45)	-0.40 (-0.40, -0.40)	-2.70, -0.40
<b>Infant-to-mother ratio</b>			
Log <sub>10</sub> TFV hair concentration ratio	1.08 (0.58)	1.21 (0.83, 1.40)	-1.36, 2.22

<sup>1</sup> For pregnancies (n=2) with infant hair level < LLOQ, the value LLOQ (=0.002 ng/mg) was used in analysis; for pregnancies with hair level > ULOQ (1 maternal hair; 82 infant hair), the value ULOQ (=0.4 ng/mg) was used in analysis.



## Future directions

- PrIMA Extension Study (PrIMA-X)
  - NIH R01HD100201
  - **Aim 1**: Quantify infant PrEP exposure *in utero* and via breastmilk among mothers using PrEP during pregnancy and breastfeeding through a paired analysis of mother-infant hair samples
  - **Aim 2**: Determine whether adverse birth and early infant outcomes differ among pregnancies with and without PrEP exposure, by trimester of exposure, and quantity of exposure (PrEP levels in hair and DBS).
  - **Aim 3**: Develop an extension cohort to evaluate whether infant PrEP exposure during pregnancy and breastfeeding is associated with bone development, neurocognitive, or growth outcomes up to 5 years



# Key PrEP in pregnancy safety gaps

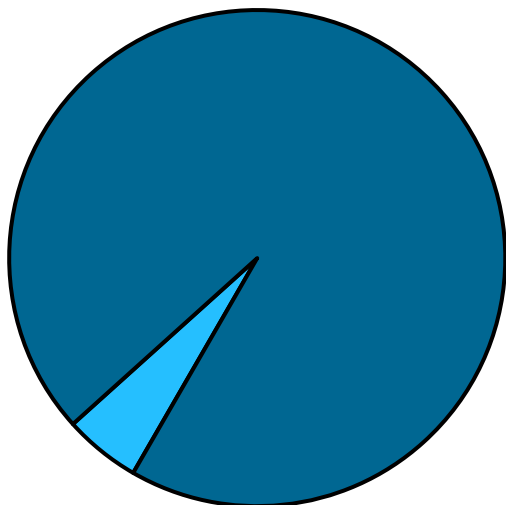
- ◆ **Few PrEP in pregnancy studies**
  - ◆ 3/5 from RCTs (PrEP stopped in pregnancy)
- ◆ **Few studies quantify infant exposure**
  - ◆ Maternal adherence also not confirmed
- ◆ **No data on longer-term outcomes**
  - ◆ Only perinatal outcomes, growth up to 1 year





# Pregnant women are...

**Excluded from 95% of drug studies, but...**



- Review of all clinicaltrials.gov Phase IV studies on medications not thought to be teratogenic
- Most studies require negative pregnancy test/contraceptives

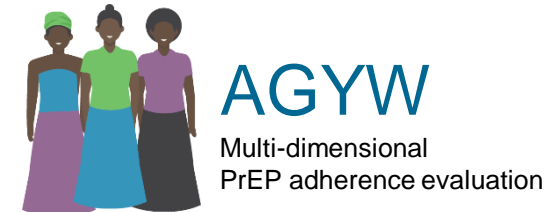
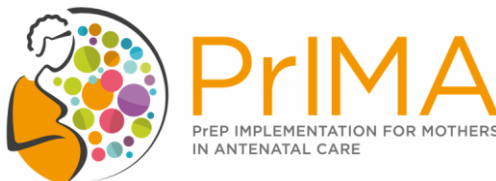
*Andrade et al Am J Obstet Gynecol 2004*  
*Shields et al Obstet Gynecol 2013*



Who will  
accept  
PrEP?

Who should  
be offered  
PrEP?

Who will  
adhere to  
PrEP?



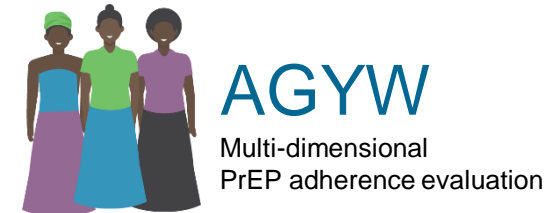
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# Integrated delivery approach



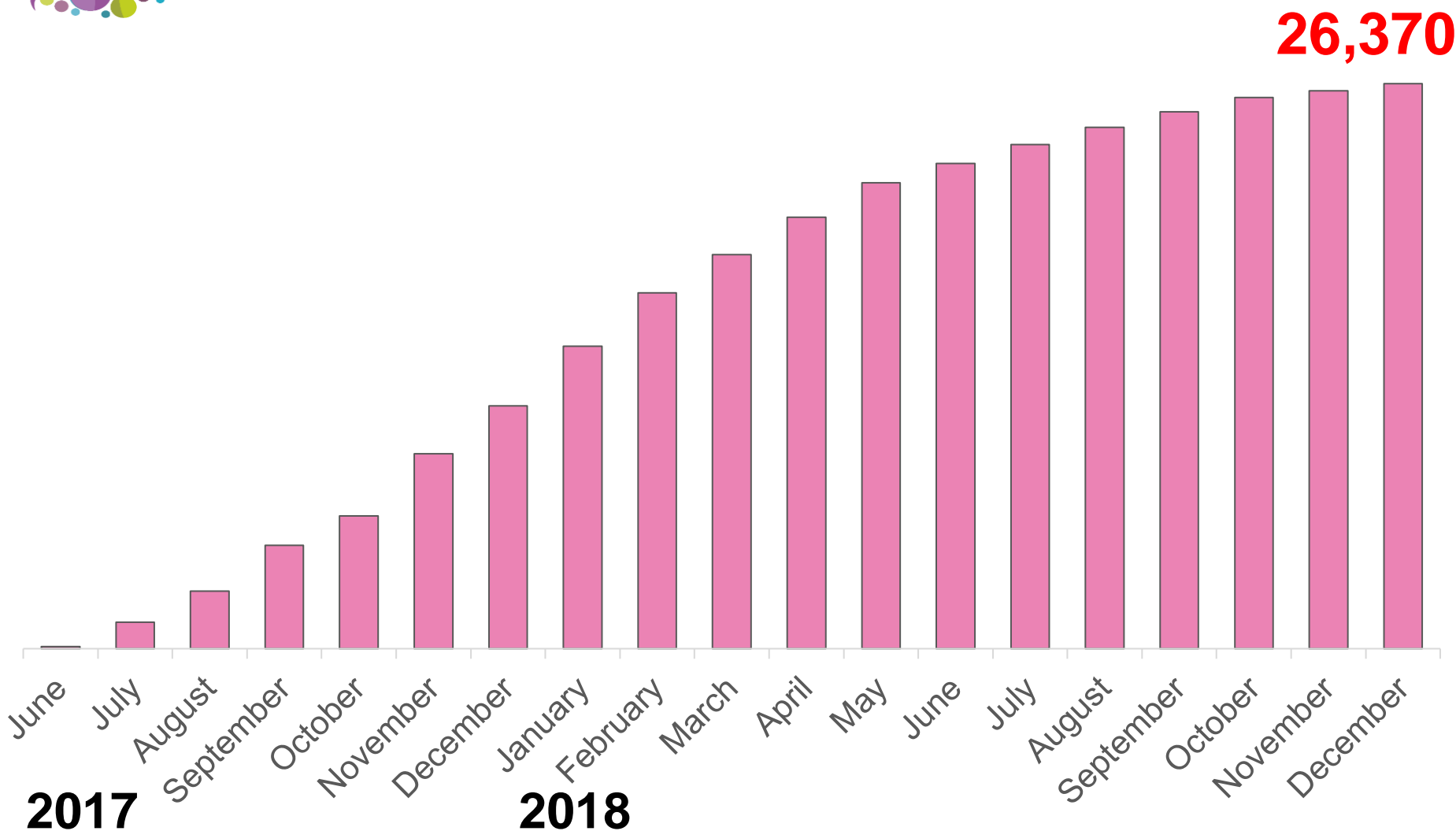






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# Cumulative no. of PrEP screenings\*

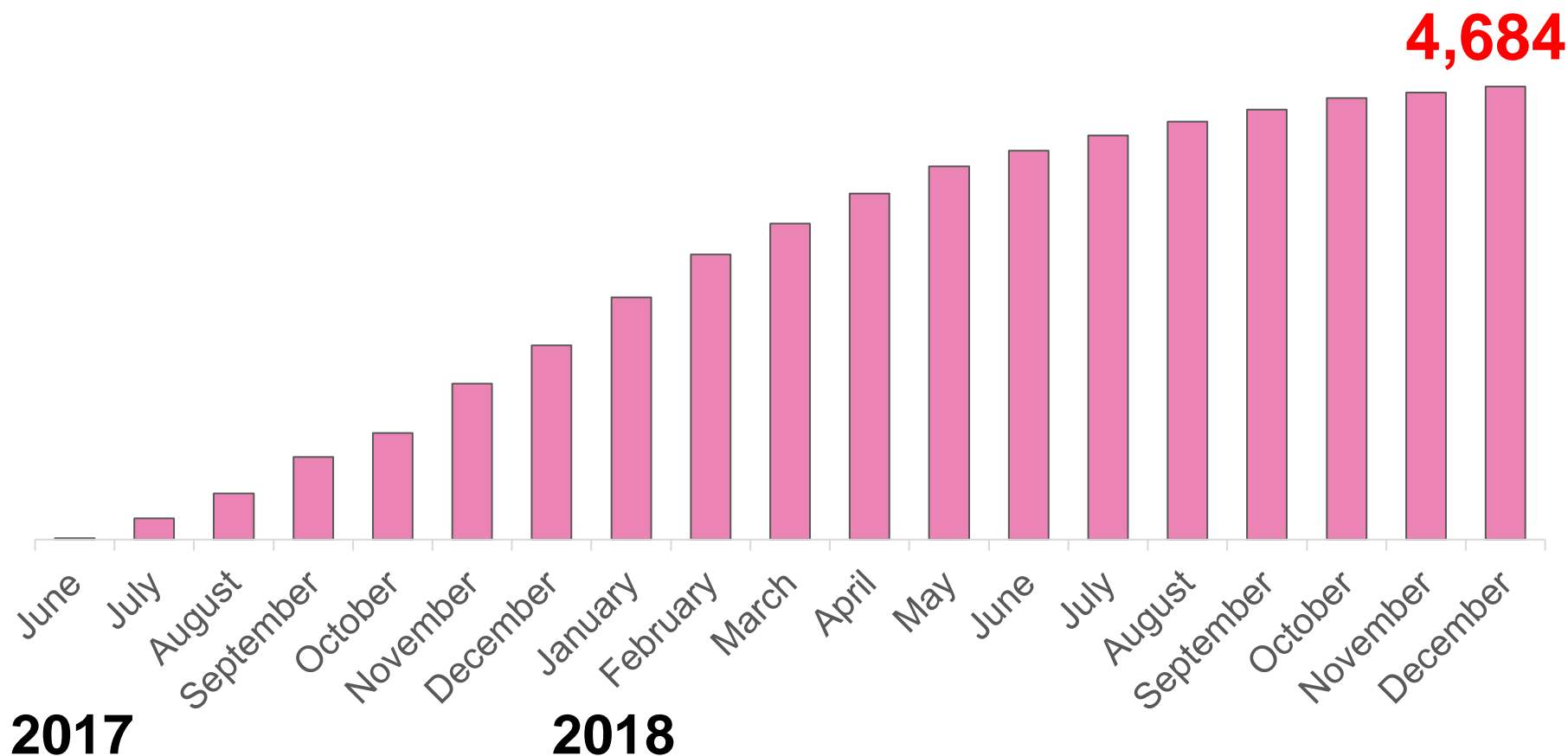


\*At 16 PriYA-dedicated sites (PriYA and facility nurses) and mentorship sites





# Cumulative no. of PrEP initiations\*



\*At 16 PriYA-dedicated sites (PriYA and facility nurses) and mentorship sites



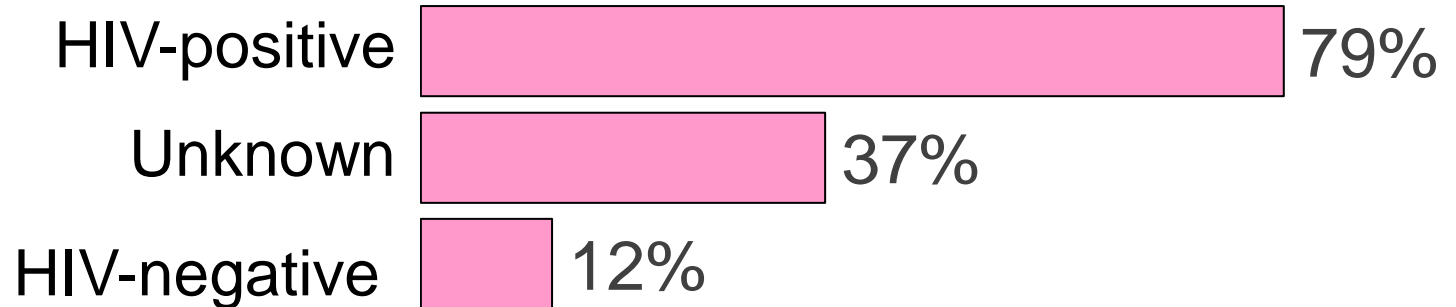




# PrEP uptake among pregnant and breastfeeding women

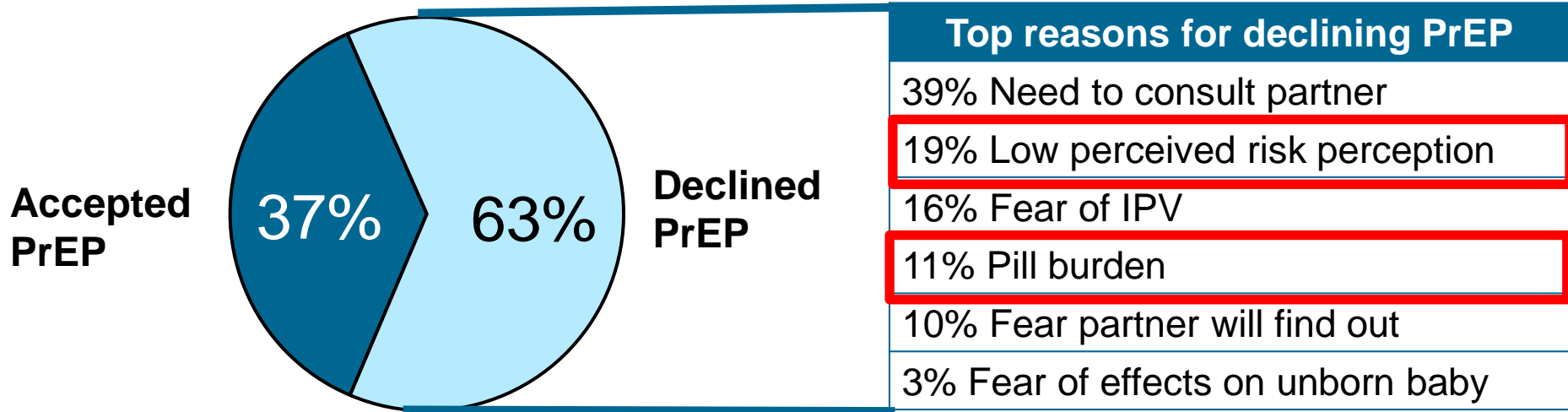
**Overall**  22%

## Male partner HIV status





# PrEP use among pregnant and breastfeeding women with male partners of unknown HIV status<sup>1</sup>



# Future Directions

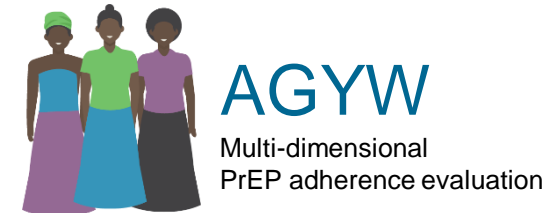
- ◆ PrIMA Point-of-Care (PrIMA-POC)
  - ◆ Supplement to NIH R01AI125498
  - ◆ Will test GeneXpert CT/NG testing as an implementation strategy to increase PrEP uptake within ANC
- ◆ mWACH-PrEP
  - ◆ NIH R01NR019220
  - ◆ Will conduct RCT to determine the effect of a 2-war SMS tool (mWACH-PrEP) on PrEP adherence during pregnancy and postpartum and we will collect data on implementation and cost to expedite translation into routine practice



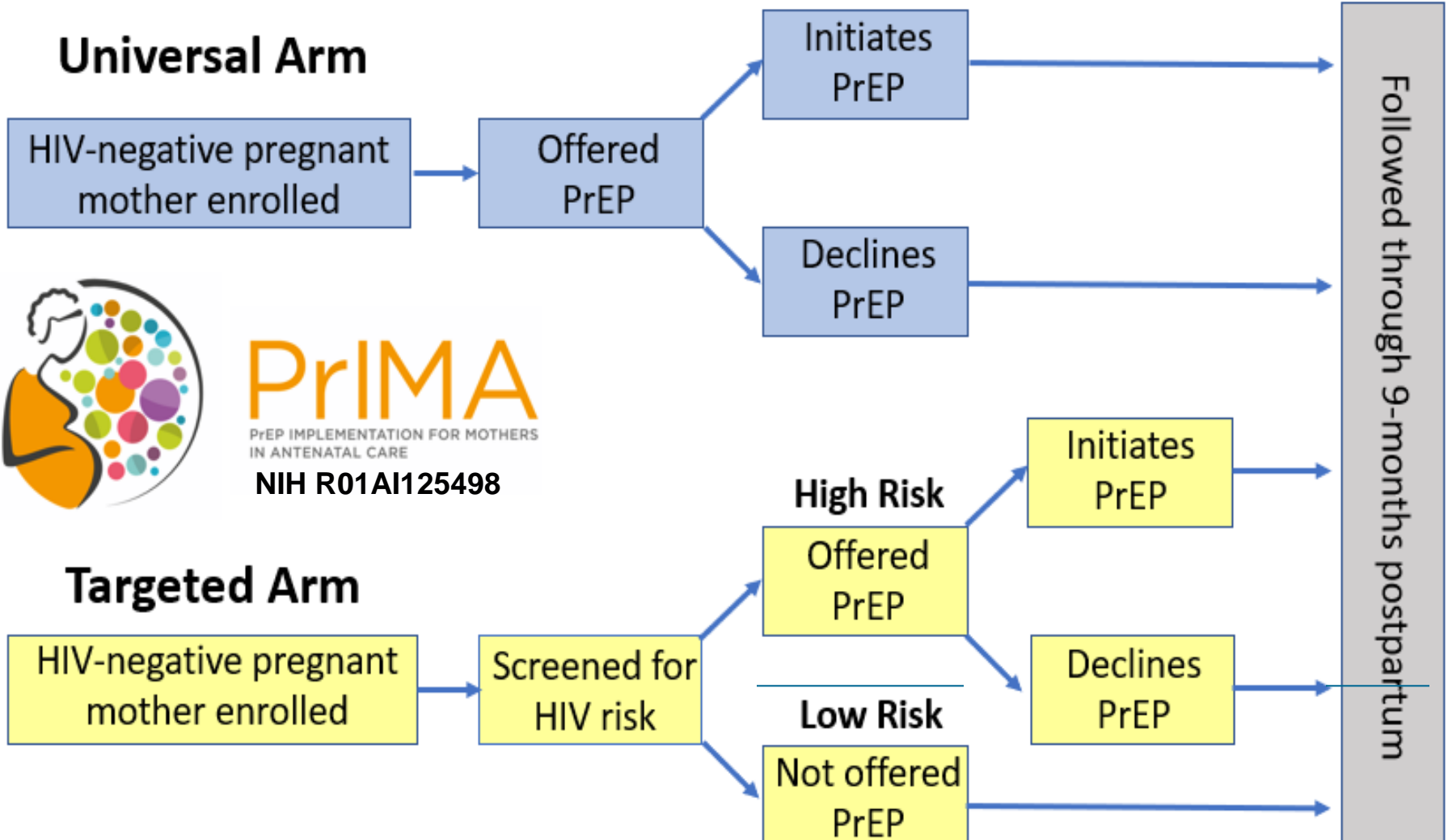
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## Universal Arm

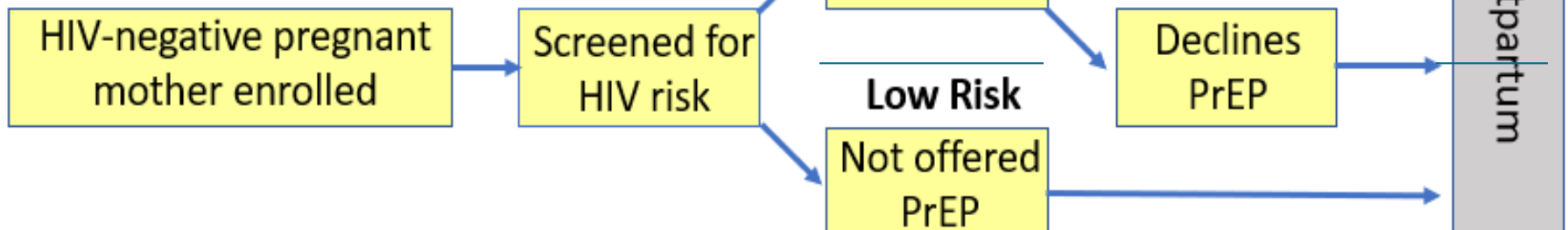


# PrIMA

PrEP IMPLEMENTATION FOR MOTHERS  
IN ANTENATAL CARE

NIH R01AI125498

## Targeted Arm



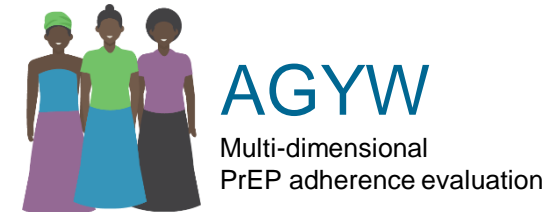
Dettinger et al *BMJ Open* 2019



Who will  
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**Pregnancy compounds adherence challenges**

*“Being that I was expectant, and you know the challenges, fatigue, morning sickness, at times I just felt so tired and you want to take this medicine (PrEP), and I had complications with my pregnancy, so I just found it very challenging to continue taking the drugs every day, with my situation”*

**Normal pregnancy supplements facilitate taking daily PrEP pills**

*“When I was pregnant taking iFAS (iron supplements), it would help me to remember (to take PrEP), I was taking it at night so I would take them all at once but now I’m used to taking it before I go to sleep”*

**Aligning PrEP and ANC visits facilitates retention**

*"That was not a challenge for me (to attend PrEP visits) because it was coincided together with my regular antenatal clinic. I knew well that I had to pass through this place for PrEP on my regular clinic day."*

**PrEP makes sex more pleasurable**

*"I enjoy sex more because I know that he cannot infect me"*

**Pintye et al IAS 2019; manuscript under review**



# IMPAACT 2009 – PK component

- Design:** Pharmacokinetic (PK) study with oral PrEP drug concentrations determined under adequate adherence conditions.
- Purpose:** To establish, among young HIV-uninfected women, plasma drug concentrations associated with daily directly observed oral PrEP during pregnancy and postpartum.
- Population:** HIV-uninfected pregnant women 16 – 24 years of age and their infants.
- Group 1:** Enrolled during pregnancy at 14 – 24 weeks' gestation
- Group 2:** Enrolled postpartum within 6 – 12 weeks after delivery
- Sample Size:** Approximately 40 women (20 per group) to achieve at least 30 evaluable women (15 per group) and their infants.

(Protocol chairs: Ben Chi, Lynda Stranix-Chibana and Sybil Hosek)





# IMPAACT 2009 – PK component

Interpretation	DBS TFV-DP fmol/punch	
	Pregnancy	Postpartum
~ 7 doses/wk	≥ 650	≥ 950
2-6 doses/wk	200-649	250-949
< 2 doses/wk	< 200	< 250

Based on 25<sup>th</sup> percentile

Interpretation	DBS TFV-DP fmol/punch	
	Pregnancy	Postpartum
~ 7 doses/wk	≥ 600	≥ 1000
2-6 doses/wk	200-599	400-999
< 2 doses/wk	< 200	< 400

Based on ROC analysis

(Protocol chairs: Ben Chi, Lynda Stranix-Chibana and Sybil Hosek; CROI 2020)



# What do we know?

- ◆ PrEP appears safe in pregnancy
- ◆ WHO recommends PrEP in pregnancy
- ◆ Pregnant women want PrEP

# What don't we know?

- ◆ Longer-term infant outcomes
- ◆ Sustained PrEP use after birth
- ◆ Impact of new PrEP agents



<https://sites.google.com/uw.edu/priya/home>



# Know PrEP, No HIV

Talk to your health care provider about whether PrEP is right for you



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**Determined**

**Resilient**

**Empowered**

**AIDS-Free**

**Mentored**

**Safe**





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# Acknowledgments



**PrIMA**  
PrEP IMPLEMENTATION FOR MOTHERS  
IN ANTENATAL CARE

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