



Landscape of PrEP in Pregnancy



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University of Washington



Global WACH
WOMAN • ADOLESCENT • CHILD • health

What do we know?

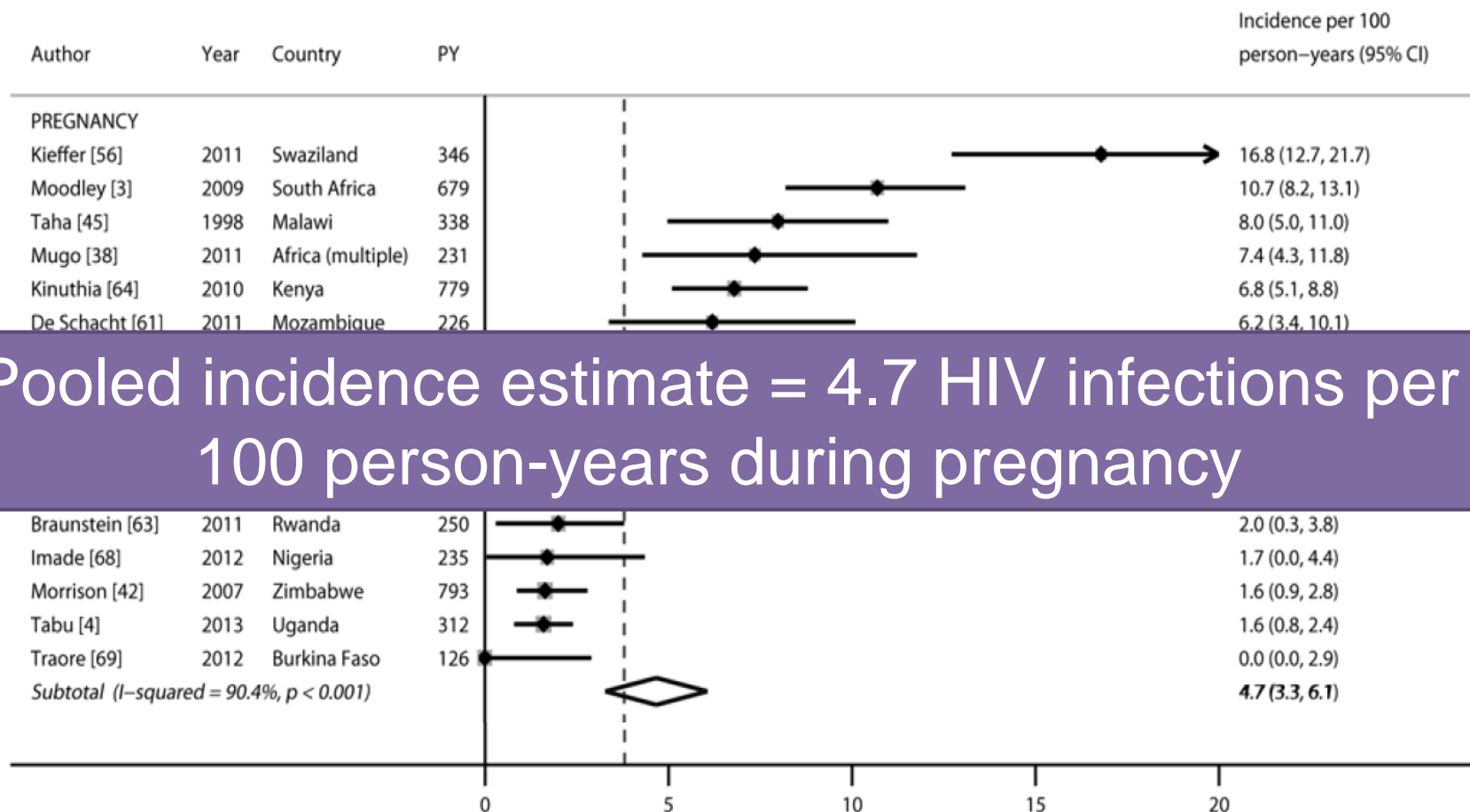
- ◆ PrEP appears safe in pregnancy
- ◆ WHO recommends PrEP in pregnancy
- ◆ Pregnant women want PrEP

What don't we know?

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



High HIV incidence during pregnancy

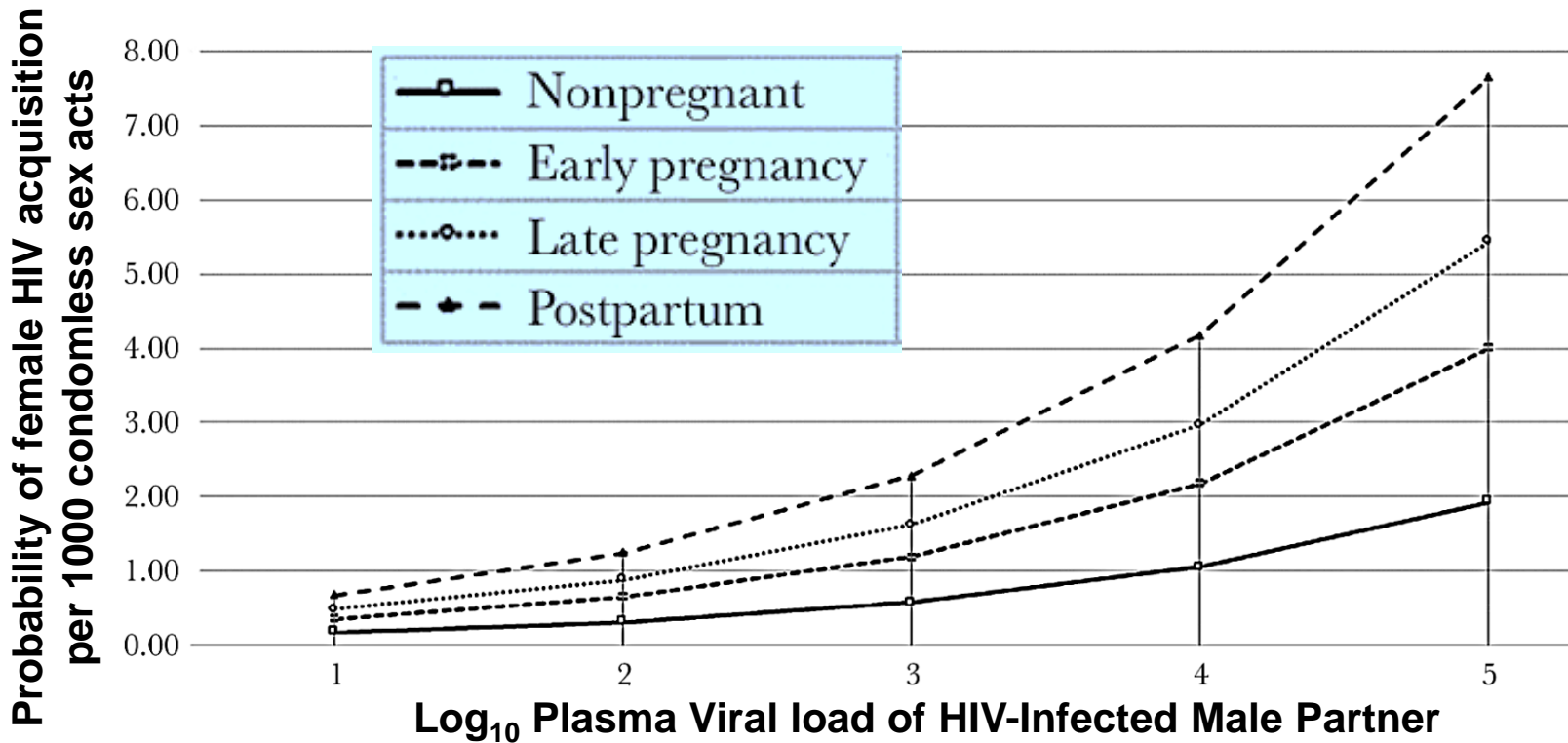


Pooled incidence estimate = 4.7 HIV infections per 100 person-years during pregnancy

Drake et al *PLOS MED* 2014



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



Thomson et al *JID* 2018





Photo credit: Paul J. Brown Photography



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^a, Rachel C. Baggaley^b and Ioannis Mameletzis^b

- ◆ 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

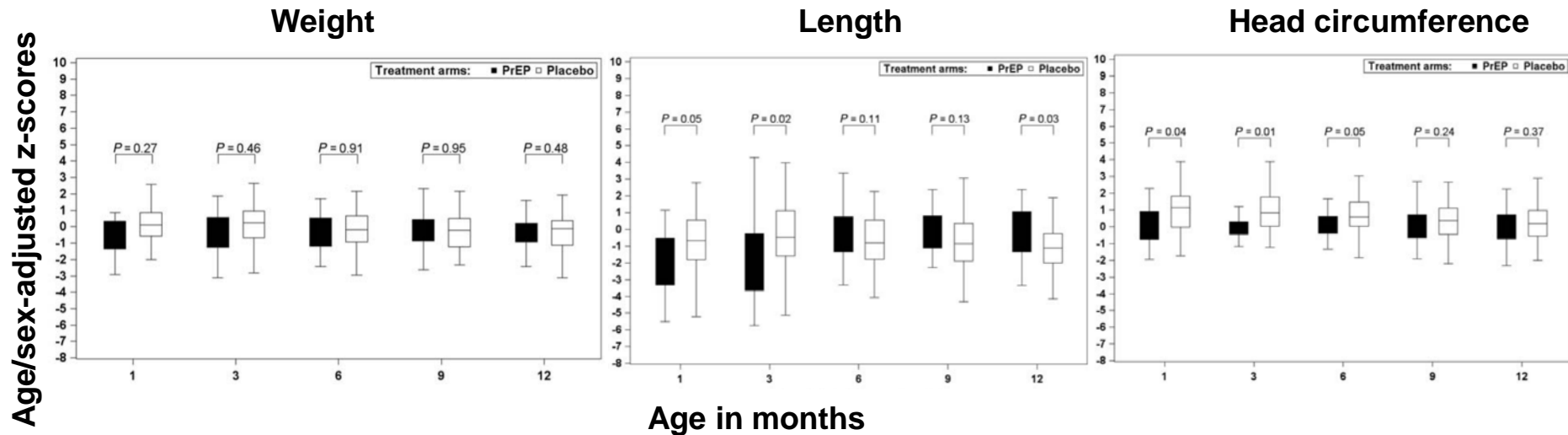
Study; Lead Author	PrEP-exposed pregnancies	Outcomes	
		Pregnancy	Infant
FEM-PrEP; Callahan 2015	n=69	No difference in outcomes by arm	None reported
Partners PrEP Study; Mugo 2014	n=335	No difference in pregnancy loss or preterm birth by arm	No difference in congenital anomalies, growth at 1-year
VOICE; 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

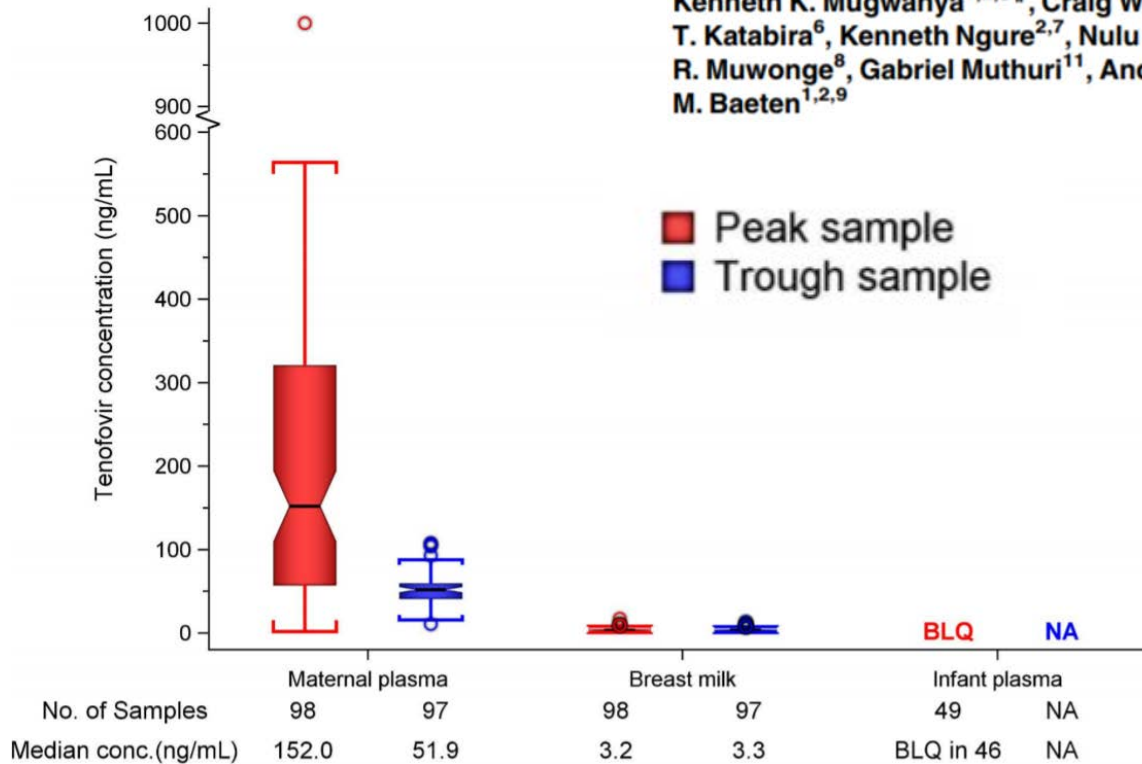
Birth outcome	PrEP exposed (n=246)	PrEP unexposed (n=7515)	p-value
Frequency of preterm birth	2.2%	3.5%	0.34
Median birth length (cm)	48	48	0.40
Median birth weight (kg)	3.4	3.3	0.01*
Congenital malformation	<1%	<1%	0.645

Dettinger et al; presented at HIVR4P 2018



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^{1,2,3,*}, Craig W. Hendrix⁴, Nelly R. Mugo^{2,5}, Mark Marzinke⁴, Elly T. Katabira⁶, Kenneth Ngunjiri^{2,7}, Nulu B. Semiyaga⁸, Grace John-Stewart^{1,2,9,10}, Timothy R. Muwonge⁸, Gabriel Muthuri¹¹, Andy Stergachis^{2,12}, Connie L. Celum^{1,2,9}, Jared M. Baeten^{1,2,9}



Mugwanya et al *PLOS Med* 2016

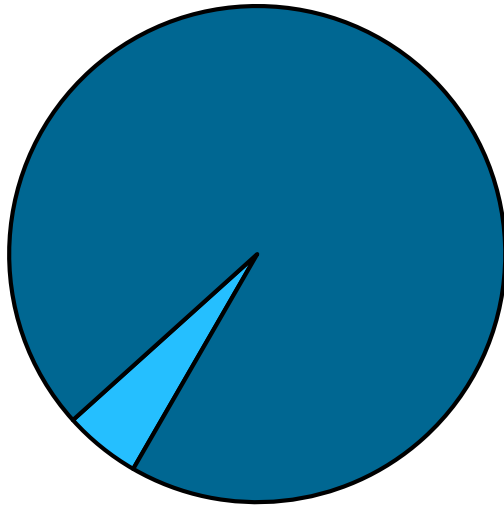
Key PrEP in pregnancy safety gaps

- ◆ **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

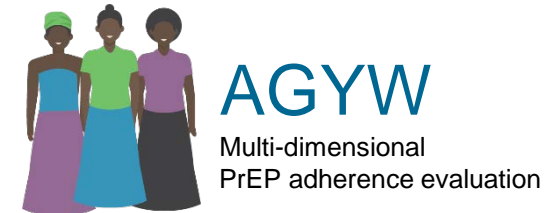
Andrade et al *Am J Obstet Gynecol* 2004
Shields et al *Obstet Gynecol* 2013



Who will
accept
PrEP?

Who should
be offered
PrEP?

Who will
adhere to
PrEP?



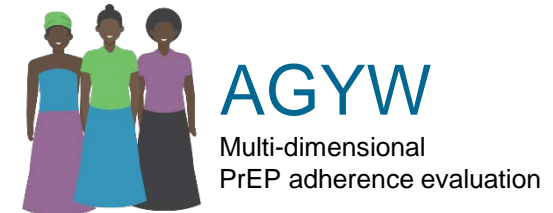
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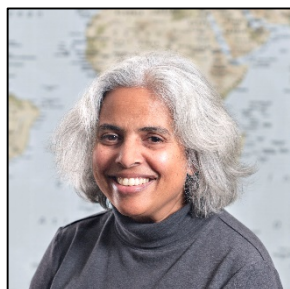




PRIYA

PrEP IMPLEMENTATION IN YOUNG
WOMEN AND ADOLESCENTS

Principal Investigators



Dr. Grace
John-Stewart



Dr. Jared Baeten



Dr. John Kinuthia





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PrEP IMPLEMENTATION IN YOUNG
WOMEN AND ADOLESCENTS

Integrated delivery approach



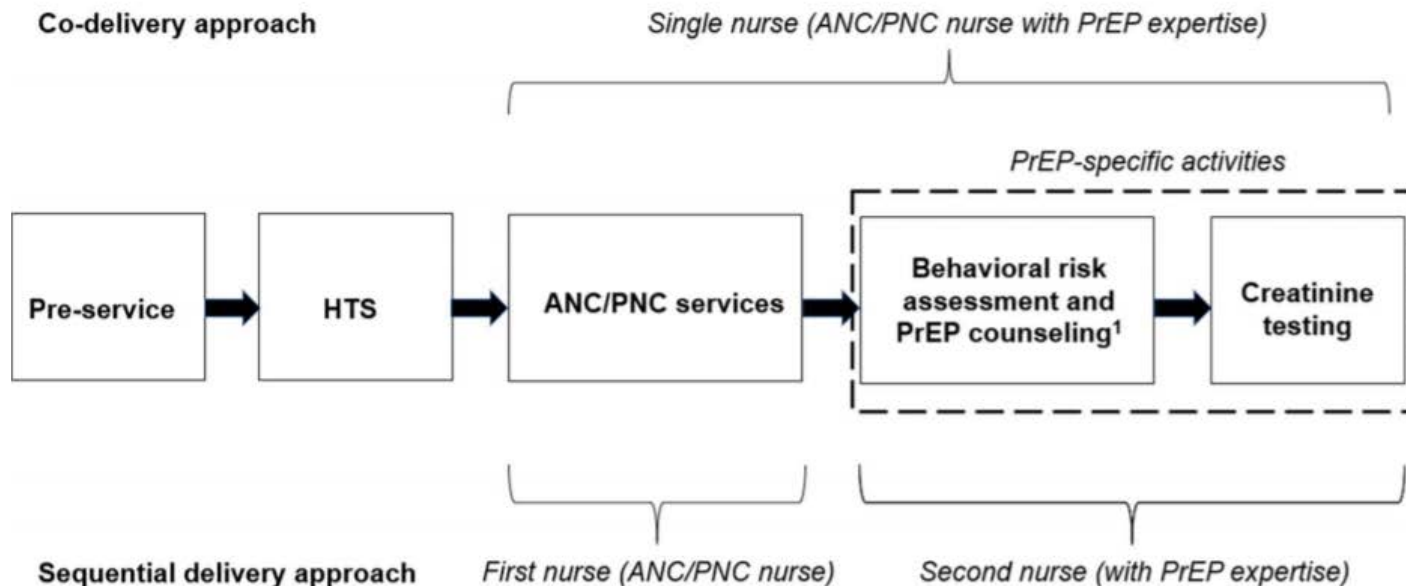
Integration of PrEP Services Into Routine Antenatal and Postnatal Care: Experiences From an Implementation Program in Western Kenya

Jillian Pintye, RN, MPH, PhD, John Kinuthia, MBChB,*† D. Allen Roberts, BS,‡*

Anjuli D. Wagner, PhD, Kenneth Mugwanya, MBChB, PhD,* Felix Abuna, BS,§ Harison Lagat, BS,§*

George Owiti, BS,§ Carol E. Levin, PhD, Ruanne V. Barnabas, MD, PhD,*‡||*

Jared M. Baeten, MD, PhD,‡|| and Grace John-Stewart, MD, PhD*‡||*





PrIYA Community Advisory Board

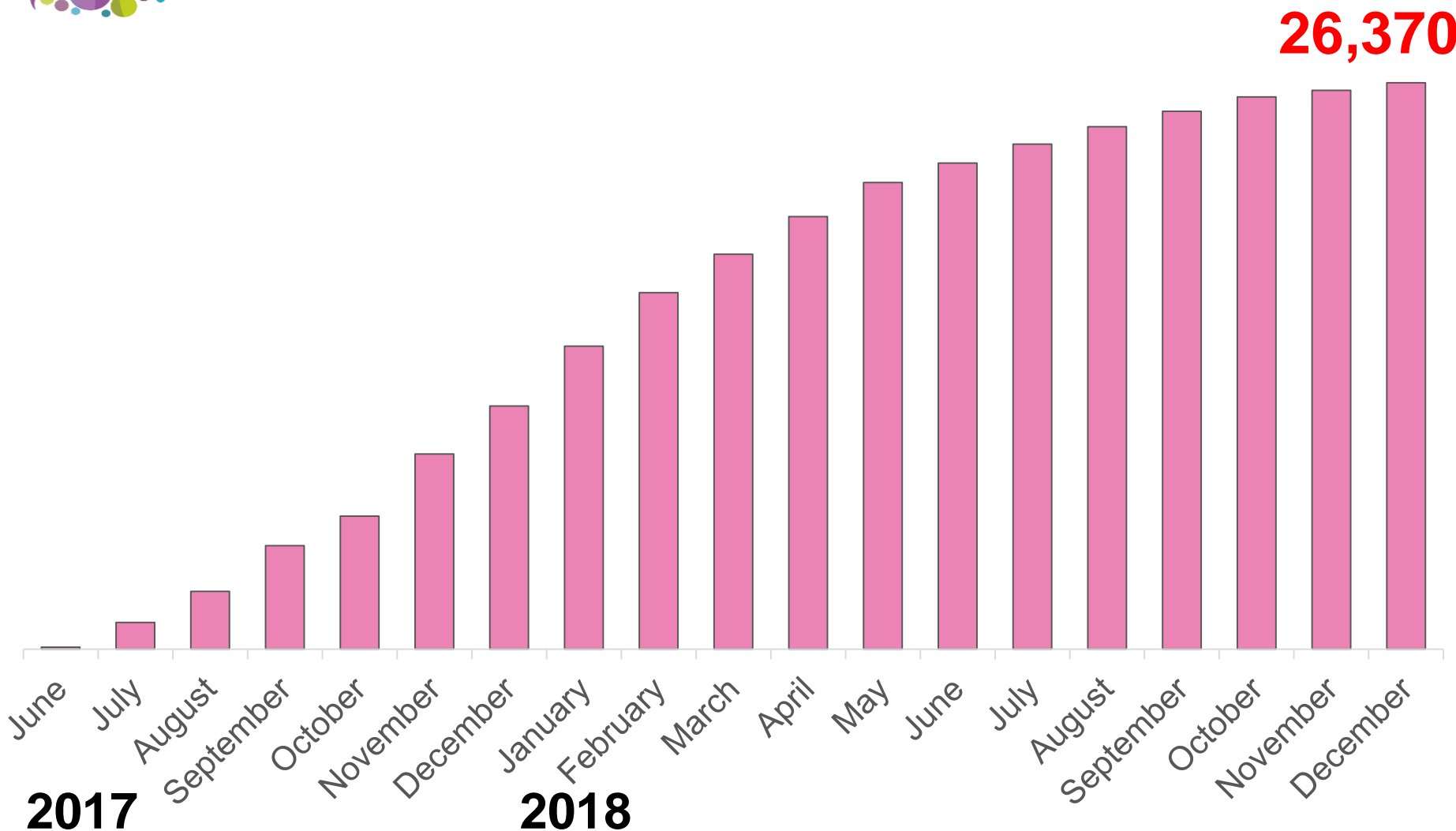






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WOMEN AND ADOLESCENTS

Cumulative no. of PrEP screenings*

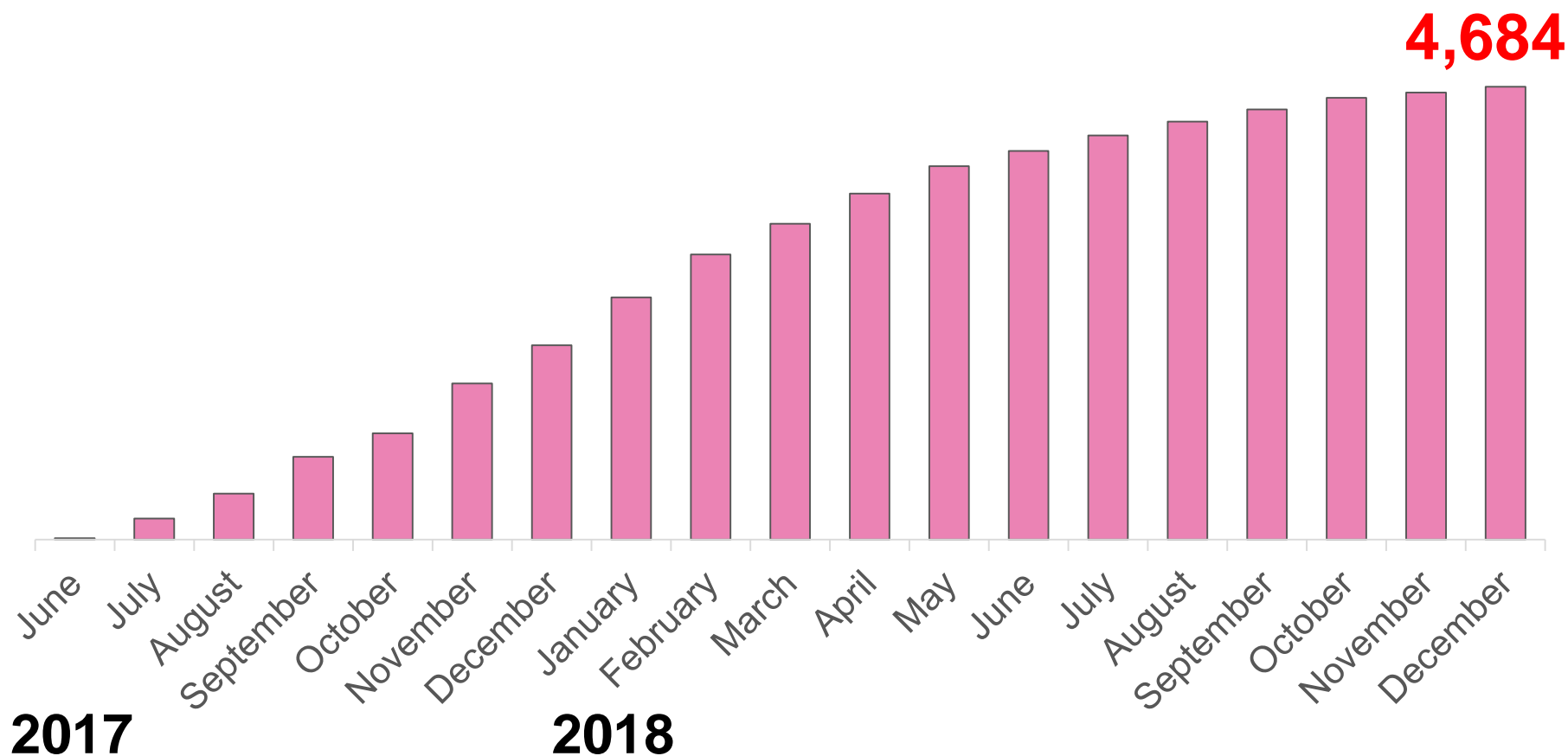


*At 16 PriYA-dedicated sites (PriYA and facility nurses) and mentorship sites



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Cumulative no. of PrEP initiations*



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

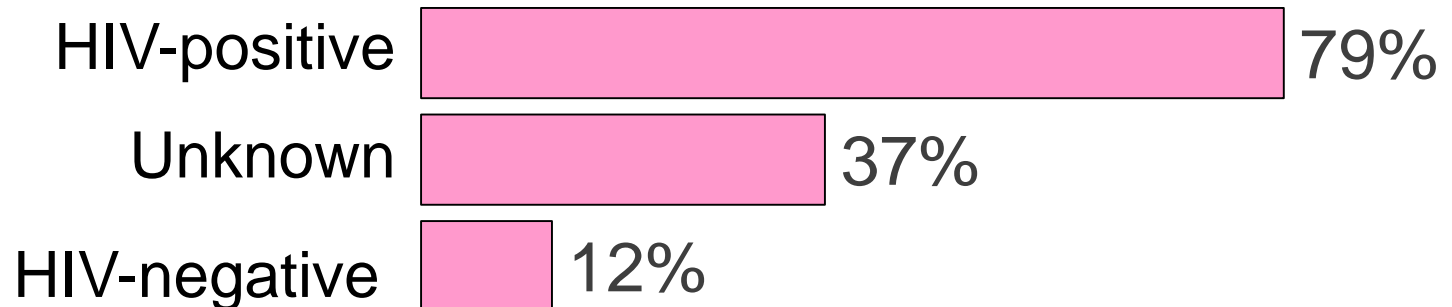


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PrEP uptake among pregnant and breastfeeding women

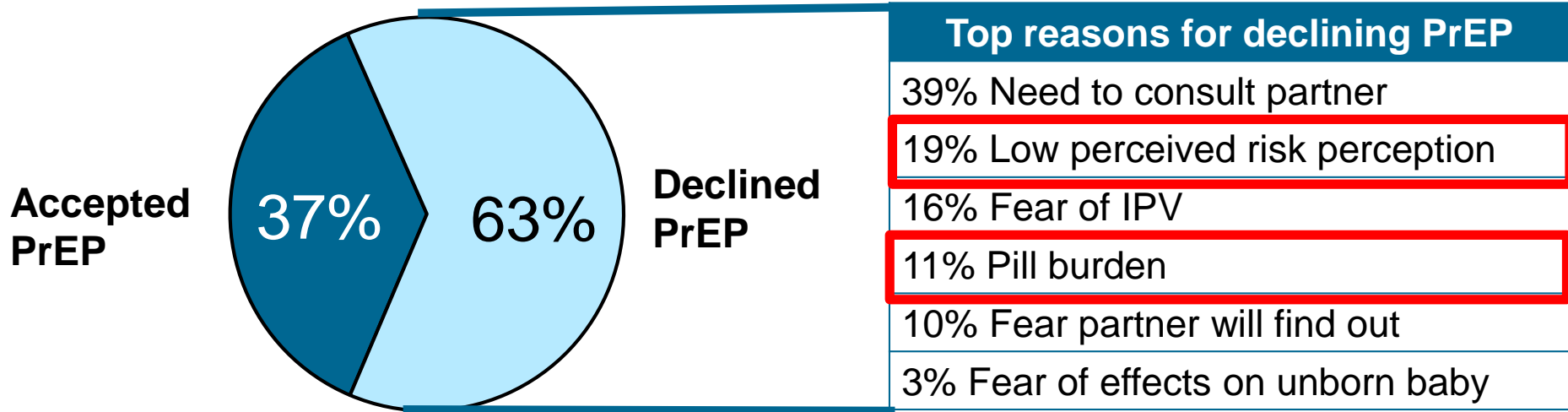
Overall  22%

Male partner HIV status





PrEP use among pregnant and breastfeeding women with male partners of unknown HIV status¹

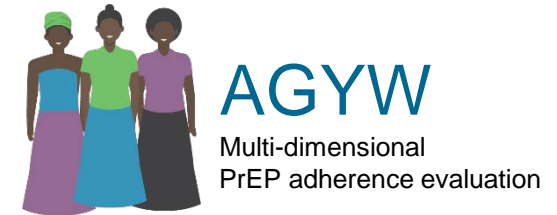
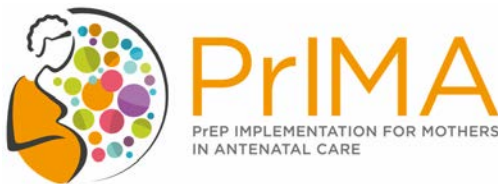




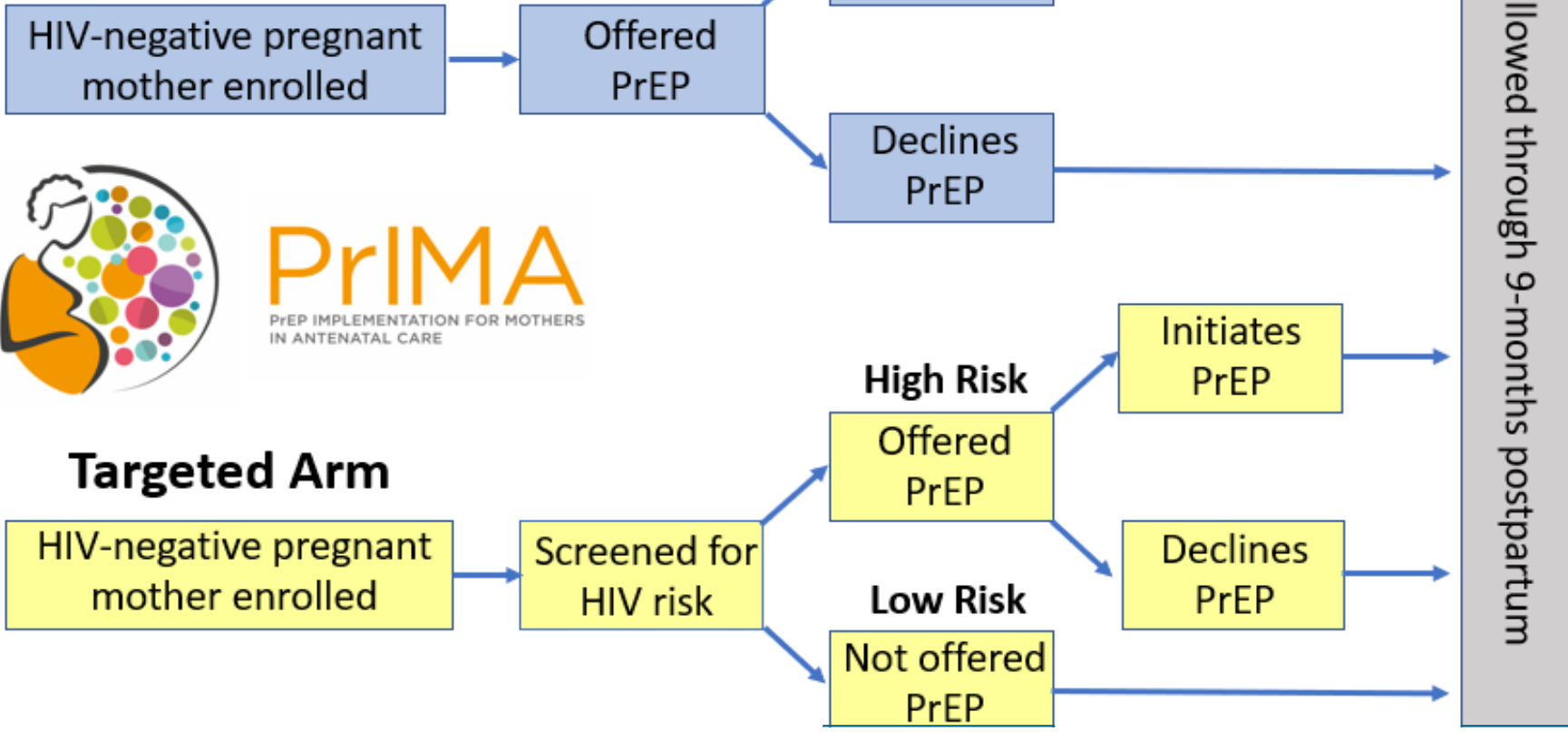
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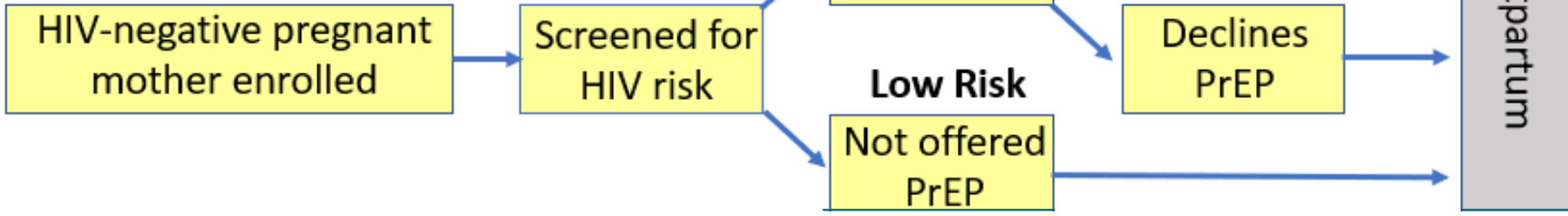


Universal Arm



PrIMA
PrEP IMPLEMENTATION FOR MOTHERS
IN ANTENATAL CARE

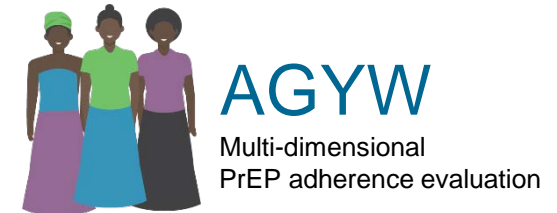
Targeted Arm



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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"



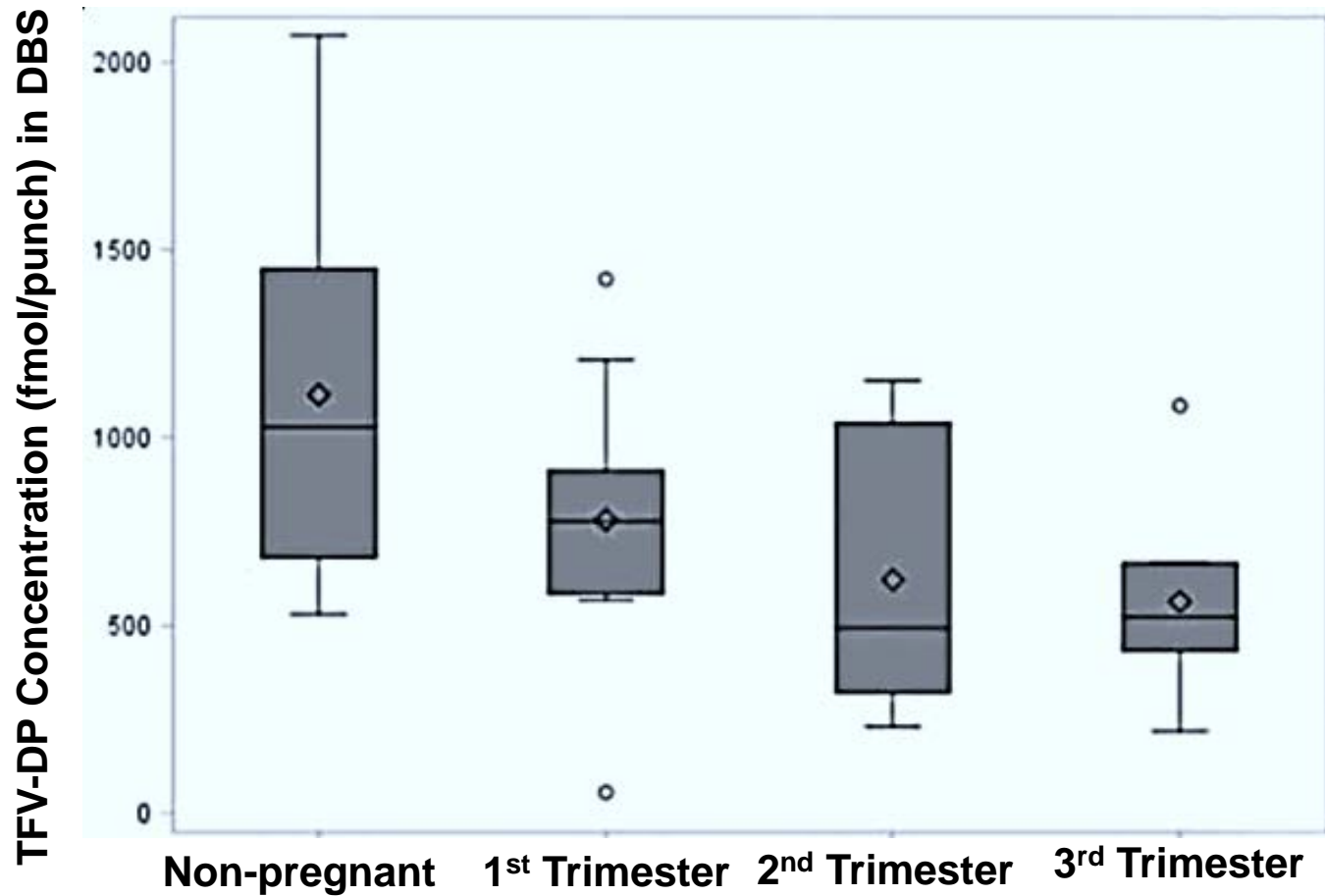
IMPAACT 2009 – PK component

- 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)



TFV-DP Levels Between Women with 100% MEMS, By Trimester



Pyra et al *AIDS* 2018



IMPAACT 2009: PrEP comparison Component

New cohort: 16-24 years, HIV-negative, <32 weeks gestations, offered 2 options:
Daily oral PrEP or No PrEP



Cohort 1:
Initiate PrEP
(n=200)

Antenatal visits:
Weeks 4, 8, 12;
then Q 12 weeks

Labor and Delivery
Week 0 (resets)

Postnatal visits:
Weeks 14 & 26

Cohort 2:
Decline PrEP
(n=100)

Antenatal visits:
Weeks 4, 8, 12;
then Q 12 weeks

Labor and Delivery
Week 0 (resets)

Postnatal visits:
Weeks 14 & 26

Intervention:

- Risk reduction counseling
- STI management
- SMS support
- Daily PrEP
- TFV-DP level-directed counseling

Evaluation:

- TFV-DP drug levels
- Adverse event monitoring including renal function/bone
- Serial HIV testing
- Behavioral risk assessment



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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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WOMEN AND ADOLESCENTS

Acknowledgments



PrIMA
PrEP IMPLEMENTATION FOR MOTHERS
IN ANTENATAL CARE

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