

PrEP in Pregnancy and Postpartum

Ongoing projects and gaps

Grace John-Stewart

IMPAACT Prevention Scientific Committee

June 13, 2019





HIV RISK



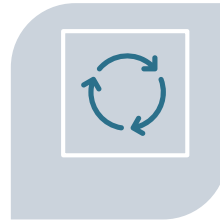
**PREP
EFFECTIVENESS**



**MOTHER'S
SAFETY**



**INFANT
SAFETY**

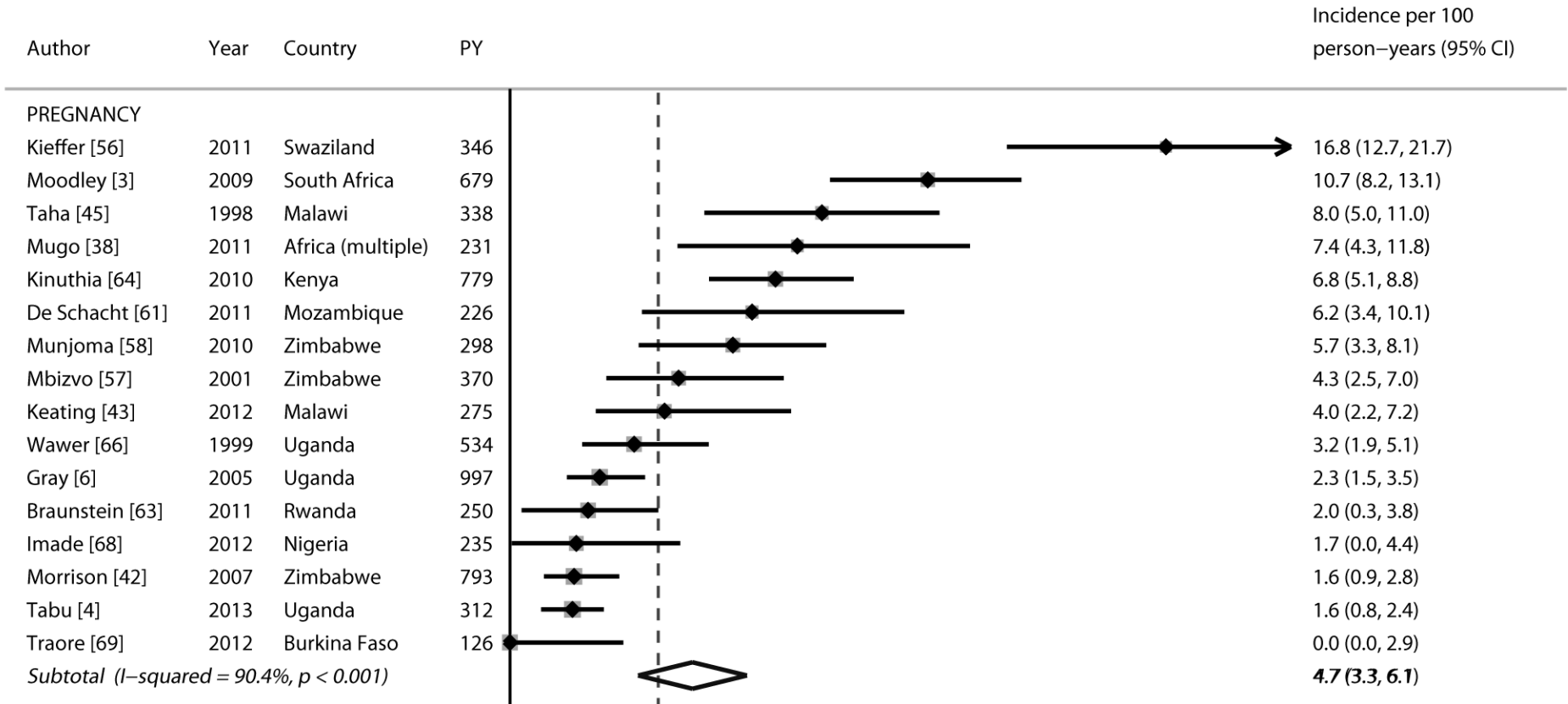


IMPLEMENTATION



Incident HIV during Pregnancy and Postpartum and Risk of Mother-to-Child HIV Transmission: A Systematic Review and Meta-Analysis

Alison L. Drake^{1*}, Anjuli Wagner², Barbra Richardson^{1,3,4}, Grace John-Stewart^{1,2,5,6}



Incident HIV during Pregnancy and Postpartum and Risk of Mother-to-Child HIV Transmission: A Systematic Review and Meta-Analysis

Alison L. Drake^{1*}, Anjuli Wagner², Barbra Richardson^{1,3,4}, Grace John-Stewart^{1,2,5,6}

Incidence per 100 person-years (95% CI)

Author Year Country PY

PREGNANCY

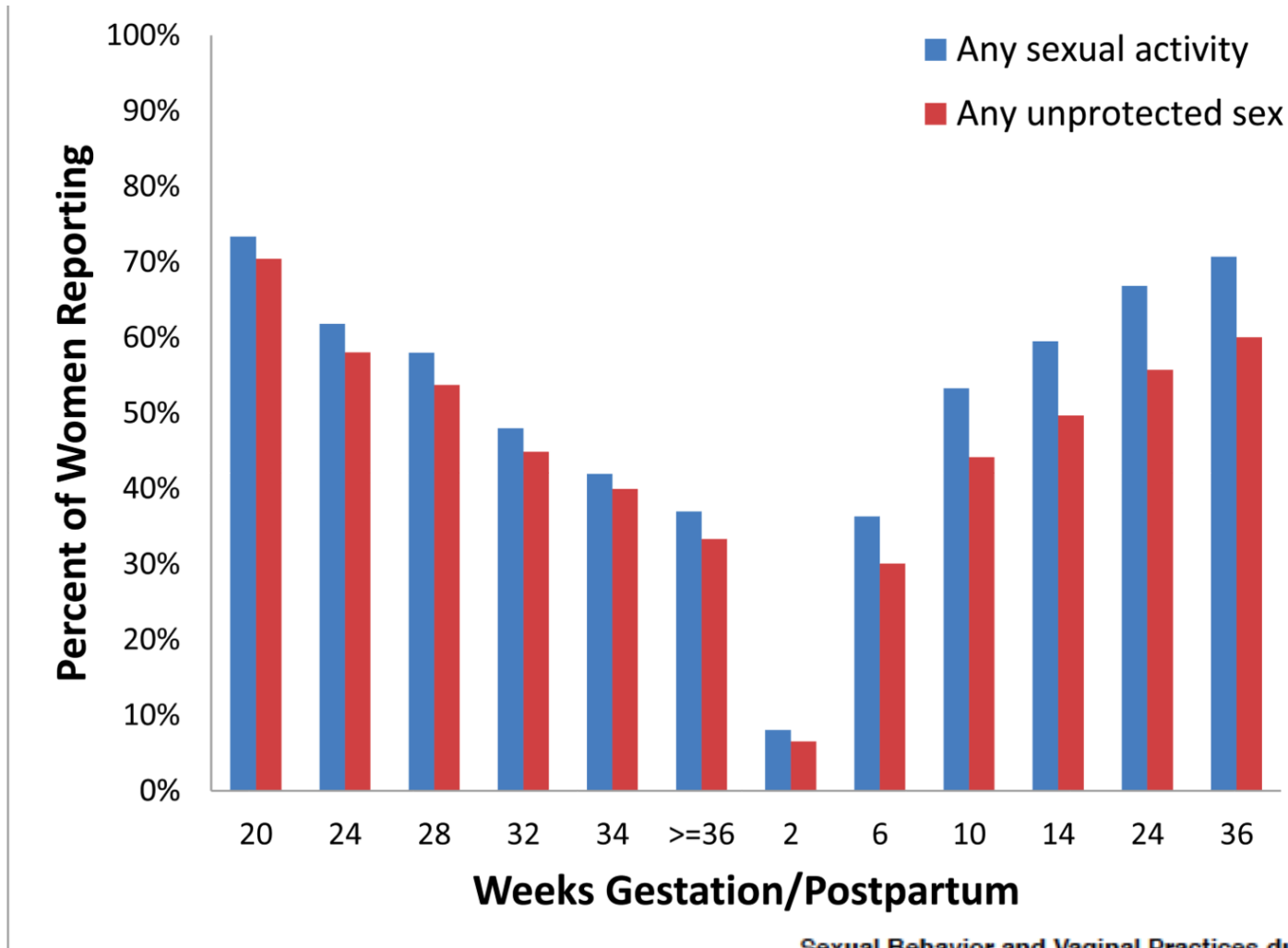
Kieffer [3]
Moodle [3]
Taha [45]
Mugo [3]
Kinuthia [3]
De Schaepwilde [3]
Munjomu [3]
Mbizvo [3]
Keating [3]
Wawer [3]
Gray [6]
Braunstein [3]
Imade [3]
Morrisson [3]
Tabu [4]

Pregnancy HIV incidence 4.7/100 py
MTCT risk 2 to 3-fold increase

Traore [69] 2012 Burkina Faso 126
Subtotal (*I*-squared = 90.4%, *p* < 0.001)



0.0 (0.0, 2.9)
4.7 (3.3, 6.1)

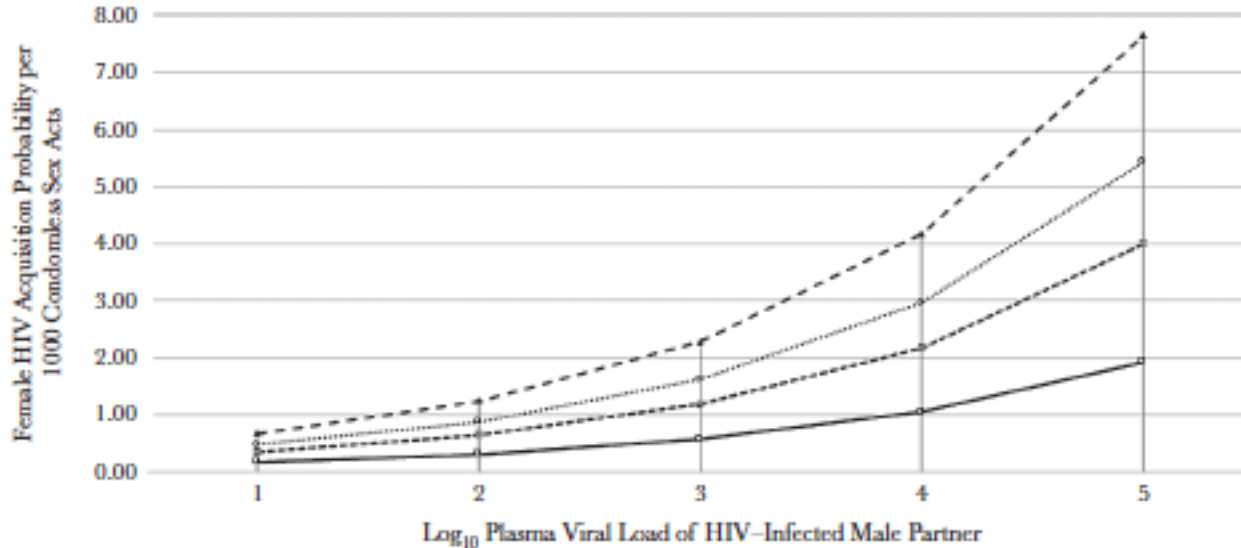


Sexual Behavior and Vaginal Practices during Pregnancy and Postpartum: Implications for HIV Prevention Strategies



Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners

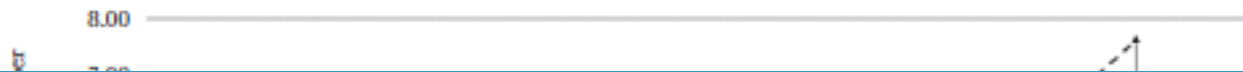
Kerry A. Thomson,¹ James Hughes,² Jared M. Baeten,^{1,3,4} Grace John-Stewart,^{1,3,4,5} Connie Colm,^{1,3,4,5} Craig R. Cohen,⁶ Kenneth Ngiro,^{1,7} James Kiari,³ Nelly Mugo,^{3,8} and Renee Heffron,^{1,9} for the Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study Teams^a



	1	2	3	4	5
— Nonpregnant	0.17	0.31	0.58	1.05	1.93
- - - Early pregnancy	0.36	0.65	1.19	2.19	4.00
... Late pregnancy	0.48	0.89	1.62	2.97	5.44
- · - Postpartum	0.68	1.25	2.29	4.18	7.65

Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners

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Pregnancy 2.8-fold higher HIV risk per-coital act
 Postpartum 4-fold higher
than non-pregnant non-postpartum women

Early pregnancy	0.36	0.63	1.19	2.19	4.00
Late pregnancy	0.48	0.89	1.62	2.97	5.44
Postpartum	0.68	1.25	2.29	4.18	7.65

PrEP in pregnancy: ongoing studies and gaps



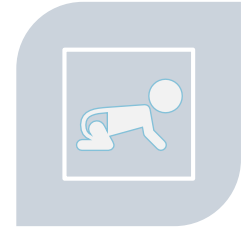
HIV RISK



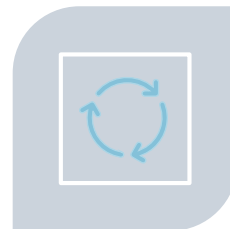
PREP
EFFECTIVENESS



MOTHER'S
SAFETY



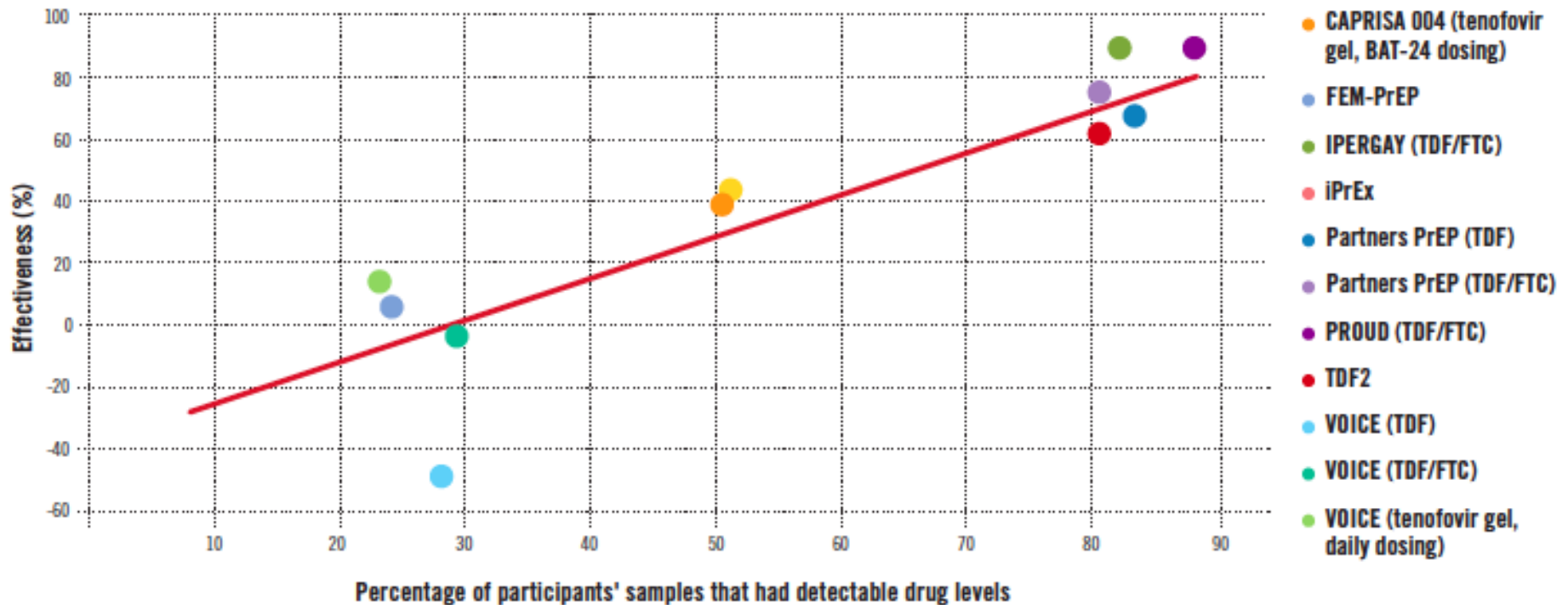
INFANT SAFETY



IMPLEMENTATION



PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



Published in final edited form as:

J Acquir Immune Defic Syndr. 2016 December 15; 73(5): 606-608. doi:10.1097/QAI.0000000000001160.

Preventing HIV-1 Infection in Women using Oral Pre-Exposure Prophylaxis: A Meta-analysis of Current Evidence

Brett Hanscom¹, Holly E. Janes¹, Peter D. Guarino¹, Ying Huang¹, Elizabeth R. Brown¹, Ying Qing Chen¹, Scott M. Hammer², Peter B. Gilbert¹, and Deborah J. Donnell¹



Preventing HIV-1 Infection in Women using Oral Pre-Exposure

Prop

Brett H
Ying Q

Study (Drug)	Region	Enrollees	Exposure	Grade	Adhere	PrEP events	Control events	Oral PrEP vs Placebo Relative Risk [95% CI]
1. FEM-PrEP (TDF/FTC)	S.Africa	Individuals	Mucosal	C	24%	33	35	0.85 [0.60, 1.52]
2. VOICE (TDF/FTC)	S.Africa	Individuals	Mucosal	C	29%	61	60	1.03 [0.73, 1.46]
3. VOICE (TDF)	S.Africa	Individuals	Mucosal	C	30%	52	35	1.49 [0.96, 2.27]
4. TDF2-Botswana (TDF/FTC)	S.Africa	Individuals	Mucosal	C	81%	7	14	0.49 [0.20, 1.21]
5. Partners PrEP (TDF/FTC)	E.Africa	Couples	Mucosal	A/C/D	77%	9	28	0.35 [0.17, 0.74]
6. Partners PrEP (TDF)	E.Africa	Couples	Mucosal	A/C/D	80%	8	28	0.30 [0.14, 0.65]
7. Bangkok (TDF)	Thailand	Individuals	Parenteral	B/AE	65%	2	9	0.32 [0.05, 1.01]

Meta-analyses Estimates, By Subgroup

(a) Southern Africa Only, Studies 1-4, (Low Adherence)	1.05 [0.78, 1.41]
(b) All Mucosal Exposure, Studies 1-6 (Mixed Adherence)	0.70 [0.42, 1.15]
(c) All Available Data, Studies 1-7 (Mixed Adherence)	0.64 [0.38, 1.05]
(d) 50%+ Adherence, Studies 4-7 (Moderate/High Adherence)	0.35 [0.22, 0.54]

Meta-analysis Regression Estimates, All Studies, By Adherence

25% Adherence	1.19 [0.89, 1.61]
50% Adherence	0.69 [0.53, 0.89]
75% Adherence	0.39 [0.25, 0.60]



Preventing HIV-1 Infection in Women using Oral Pre-Exposure

Prop

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2. VOICE (TDF/FTC)	S.Africa	Individuals	Mucosal	C	29%	81	80	1.03 [0.73, 1.48]

PrEP protective in women with moderate-high adherence (OR 0.35)



POLICY BRIEF

PREVENTING HIV DURING PREGNANCY AND BREASTFEEDING IN THE CONTEXT OF PREP

JULY 2017



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

Mofenson, Lynne M.; Baggaley, Rachel C.; Mameletzis, Ioannis

AIDS: January 14th, 2017 - Volume 31 - Issue 2 - p 213–232

doi: 10.1097/QAD.0000000000001313

CLINICAL SCIENCE

PREVENTING HIV
DURING PREGNANCY
AND BREASTFEEDING IN
THE CONTEXT OF PrEP

No evidence to support prohibiting or
discontinuing PrEP in pregnancy



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CLINICAL SCIENCE

Tenofovir and tenofovir-diphosphate concentrations during pregnancy among HIV-uninfected women using oral preexposure prophylaxis

Pyra, Maria^{a,b}; Anderson, Peter L.^e; Hendrix, Craig W.^f; Heffron, Renee^{a,b}; Mugwanya, Kenneth^b; Haberer, Jessica E.^{g,h}; Thomas, Katherine K.^b; Celum, Connie^{a,b,c}; Donnell, Deborah^{b,i}; Marzinke, Mark A.^f; Bukusi, Elizabeth A.^{b,d,j}; Mugo, Nelly R.^{b,j}; Asimwe, Stephen^k; Katabira, Elly^l; Baeten, Jared M.^{a,b,c} for the Partners Demonstration Study Team

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EPIDEMIOLOGY AND SOCIAL



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EPIDEMIOLOGY AND SOCIAL

TFV and TFV-DF levels lower in pregnancy



■ Overall (n=1789)
 ■ Non-pregnant (n=991)
 ■ Pregnant (n=798)

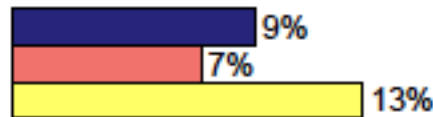


PRIYA
 PREP PREVENTION IN YOUNG
 WOMEN AND ADOLESCENTS

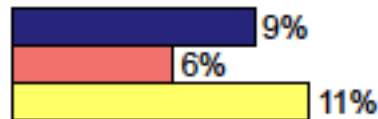
Any side effects



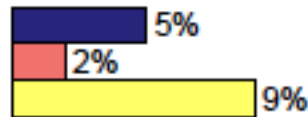
Any gastrointestinal side effects**



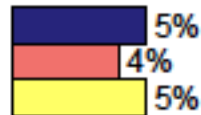
Nausea**



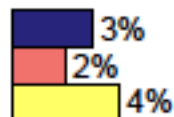
Vomiting*



Headaches*



Dizziness



*p<0.05; **p<0.001;
¹ Among women who initiated PrEP and attended 1st follow up visit



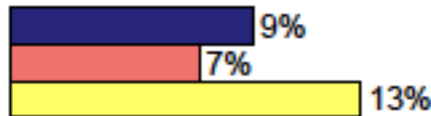
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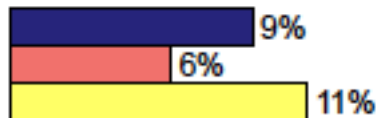
Any side effects



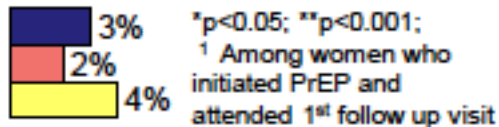
Any gastrointestinal side effects**



Nausea**



More side-effect related PrEP discontinuations in pregnant than non-pregnant women



PrEP in pregnancy: ongoing studies and gaps



HIV RISK



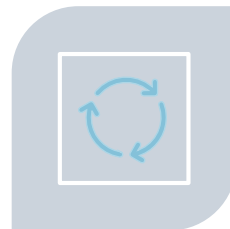
PREP
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MOTHER'S
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INFANT SAFETY



IMPLEMENTATION



	Design	#pregnancies	PrEP exposed	Difference in pregnancy or infant outcomes
Partners PrEP	RCT	431	335	None
FemPrEP	RCT	115	69	None
VOICE	RCT	452	263	None
Partners Demo	Program	126	30	Early z-score decrease
PriYA	Program	4680	246	None



	Design	#pregnancies	PrEP exposed	Difference in pregnancy or infant outcomes
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Partners	RCT	431	335	None
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5 completed studies, 1042 PrEP exposed
no increase in adverse outcomes

Davey et al., in preparation

Partners	Program	120	80	Early Z score decrease
Demo				
PriYA	Program	4680	246	None



Study	N, PrEP exposed	Maternal	Infant
PrIMA	800	Pregnancy outcomes	Growth, mortality
MPYA	71	Pregnancy outcomes	Infant mortality, congenital abn
IMPAACT 2009	300	Pregnancy outcomes, BMD	BMD, Cr, growth
PrEP-PP	720	Pregnancy outcomes	Growth, mortality, congenital abn
ZINC	120	Birth outcomes	
PrEP imm vs. deferred SA	842	Pregnancy outcomes, Cr, BMD	BMD, growth
PrEP-P	40	Pregnancy outcomes, Cr, BMD	BMD, Cr, mitochondrial
EMBRACE	550	Pregnancy outcomes	Growth, congenital malformations
PrEP observational	99	Pregnancy outcomes	Congenital malformations



Study	N, PrEP exposed	Maternal	Infant
PrIMA	800	Pregnancy outcomes	Growth, mortality
MPYA	71	Pregnancy outcomes	Infant mortality, congenital abn
IMPAACT 2009	300	Pregnancy	BMD, Cr, growth

9 ongoing or new studies, 6200 PrEP exposed with maternal and infant outcomes
Davey et al., in preparation

deferred SA		outcomes, Cr, BMD	
PrEP-P	40	Pregnancy outcomes, Cr, BMD	BMD, Cr, mitochondrial
EMBRACE	550	Pregnancy outcomes	Growth, congenital malformations
PrEP observational	99	Pregnancy outcomes	Congenital malformations





HIV RISK



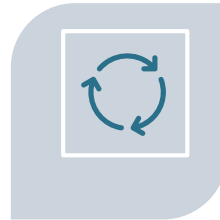
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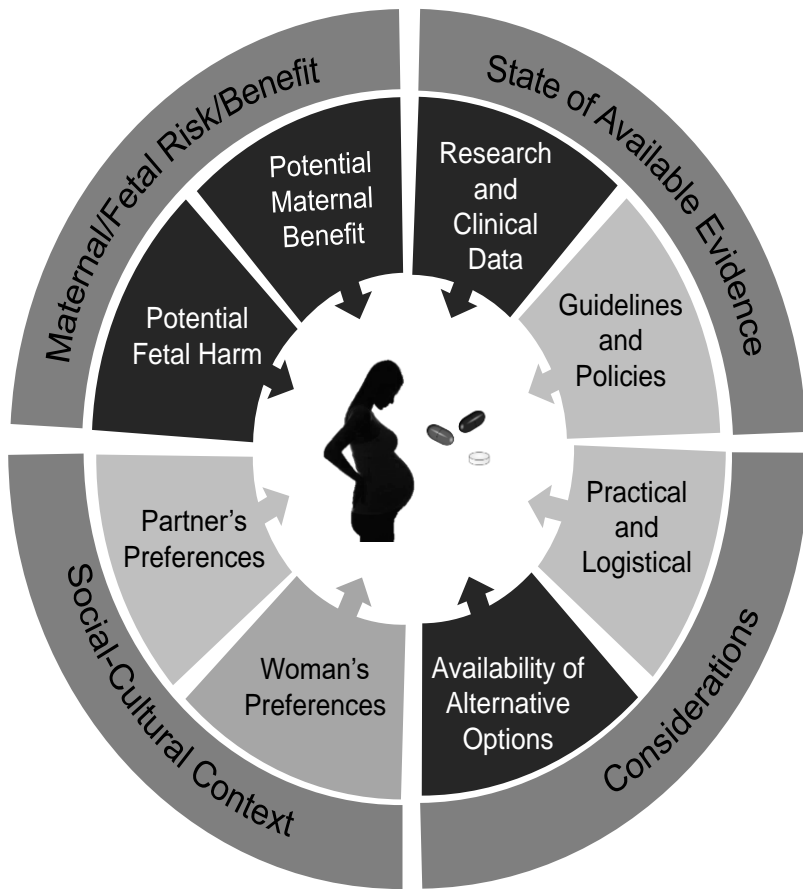


**INFANT
SAFETY**



IMPLEMENTATION





- *Women are at risk because the husbands will sleep around with other women and come back once she has given birth.*
- *If it was me I could use them secretly because if I do it in the open people will start gossiping me that I am HIV positive.*
- *I cannot use them because these drugs are for the ones with the virus... if it is ARV use by positive people, if I am not positive I will not use.*
- *I think it is a good idea because you can never trust a man, not even yourself, so if I can be given that medicine, I will sacrifice to take it so that I don't get infection.*
- *That moment you start using this drug your husband will start questioning where you came from with the virus and you have brought death to his house*

PrEP Implementation for Pregnancy and Postpartum



Universal, prevalence or risk-guided implementation



Include partner HIV self-test option to define risk



Delivery point – MCH, FP, CCC clinics or pharmacies



Self-test for serial testing



Address HCW workload, attitudes to PrEP



Standardize messaging and counseling



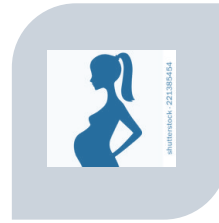
Incorporate surveillance



HIV RISK



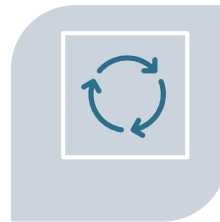
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