IMPAACT 2009:

Understanding the safety and acceptability of daily oral PrEP in pregnancy and postpartum

Benjamin Chi, MD, MSc

University of North Carolina at Chapel Hill

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International Maternal Pediatric Adolescent AIDS Clinical Trials Network

ANNUAL MEETING

2024

Key Messages

1. IMPAACT 2009 evaluated daily oral PrEP in pregnancy and postpartum through rigorous safety and adherence monitoring
2. This was one of the first DAIDS network studies focused on primary maternal HIV prevention during pregnancy and postpartum
3. Findings can inform broader implementation strategies—for this and other PrEP modalities

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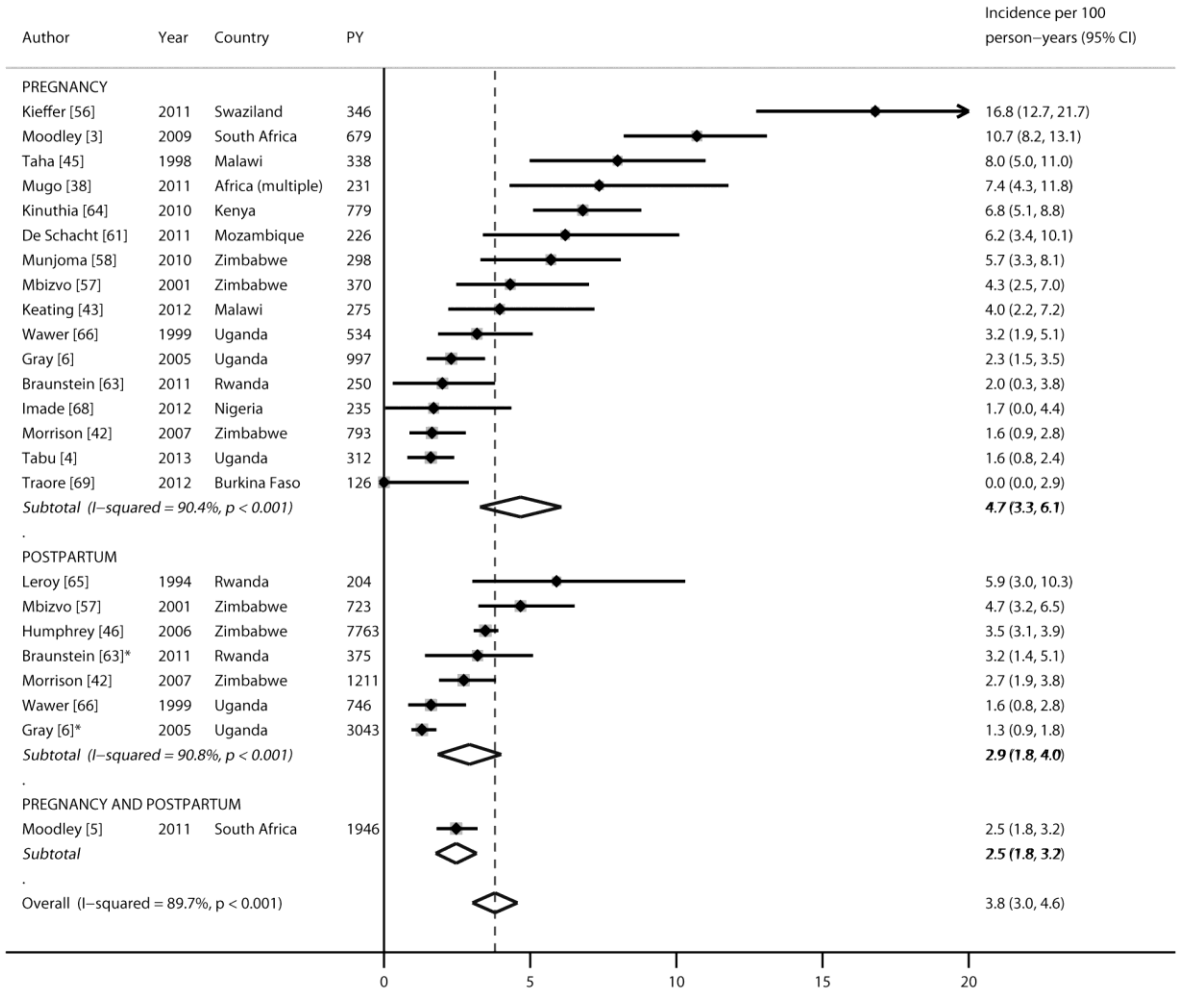
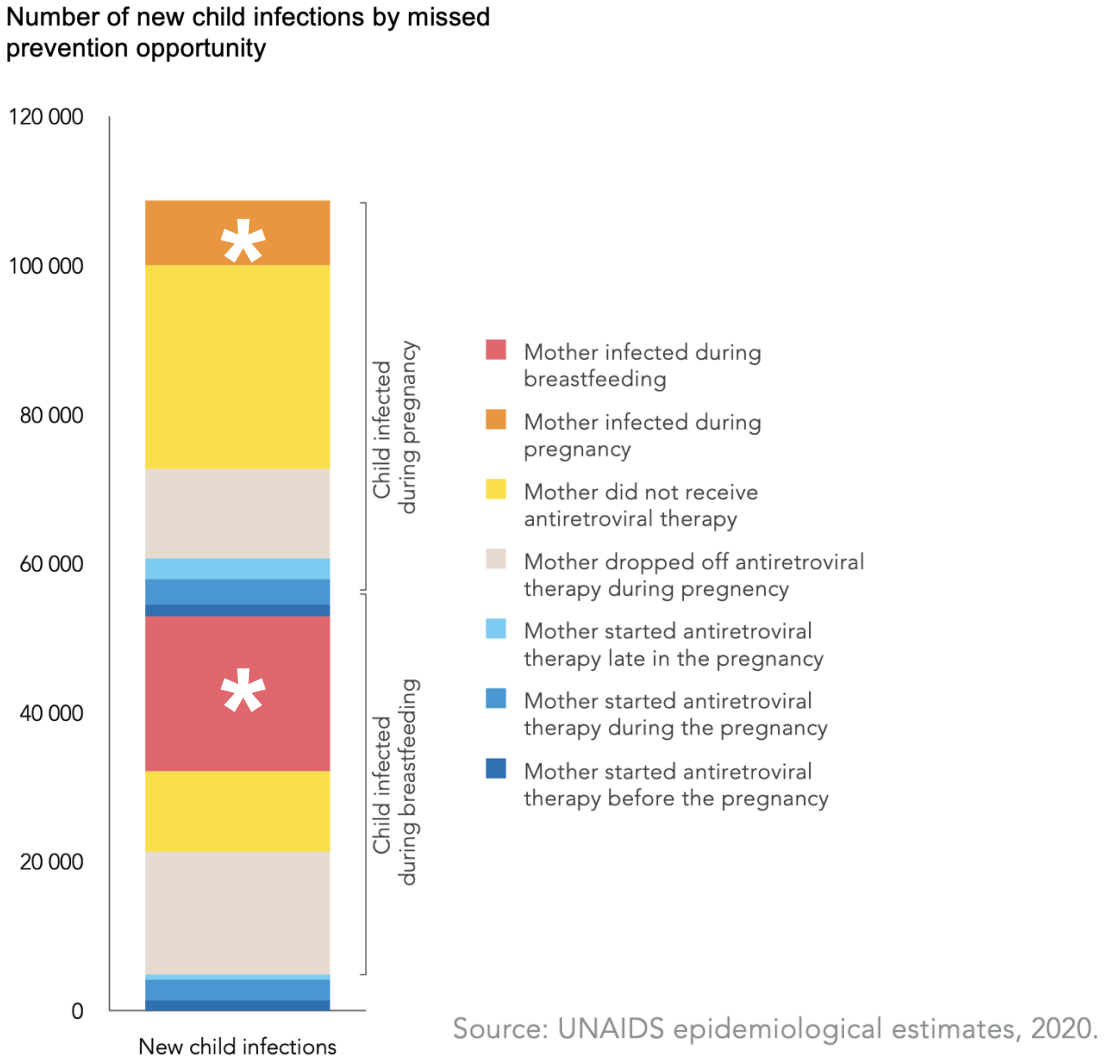
In many parts of Africa, HIV incidence is high during pregnancy and postpartum



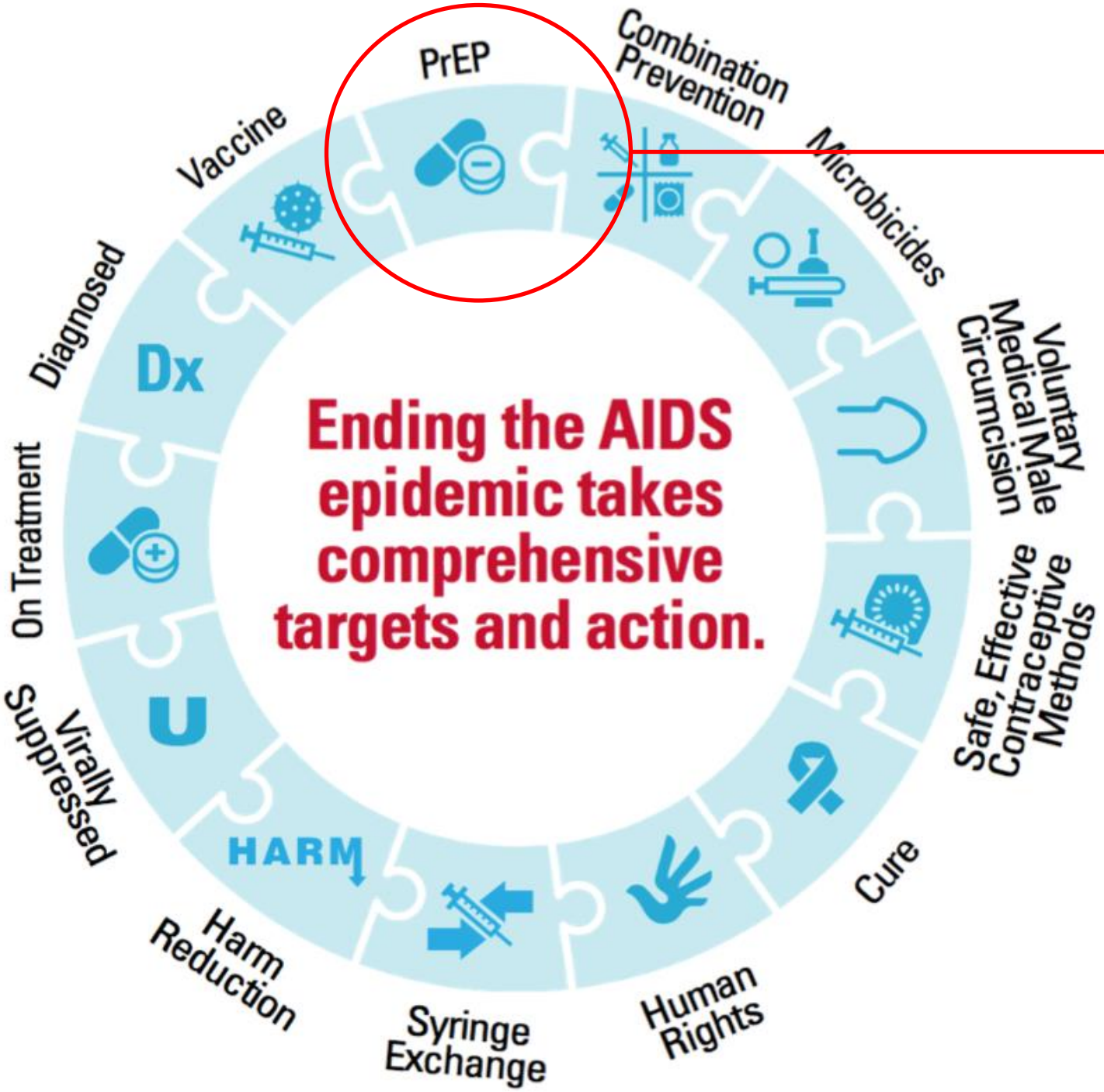
Meta-analysis of 19 cohorts (22,908 person-years)
Cumulative HIV incidence: 3.8 per 100 person-years

Drake, PLOS Med, 2014



Source: UNAIDS epidemiological estimates, 2020.

Alongside increased maternal morbidity and mortality, this contributes to greater pediatric HIV burden



Pre-exposure prophylaxis for HIV

- Medicine or product used to prevent disease in the period of risk exposure
- In pregnancy, emtricitabine/ tenofovir disoproxil fumarate (FTC/TDF) chosen for favorable profile
- Efficacious, but requires strict adherence
- Safety data in pregnancy and postpartum—especially in the context of HIV prevention–are often delayed

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IMPAACT 2009

Pharmacokinetics, Feasibility, Acceptability, and Safety of Oral Pre-Exposure Prophylaxis for Primary HIV Prevention during Pregnancy and Postpartum in Adolescents and Young Women and their Infants

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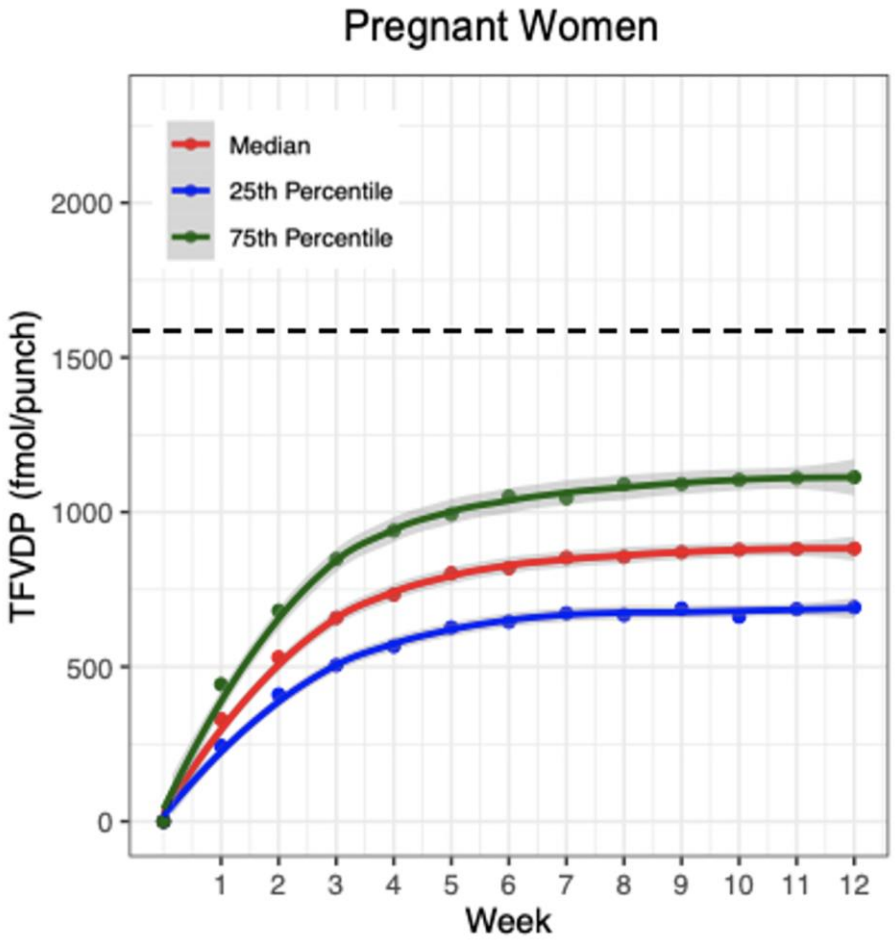
Pharmacokinetics (2019)

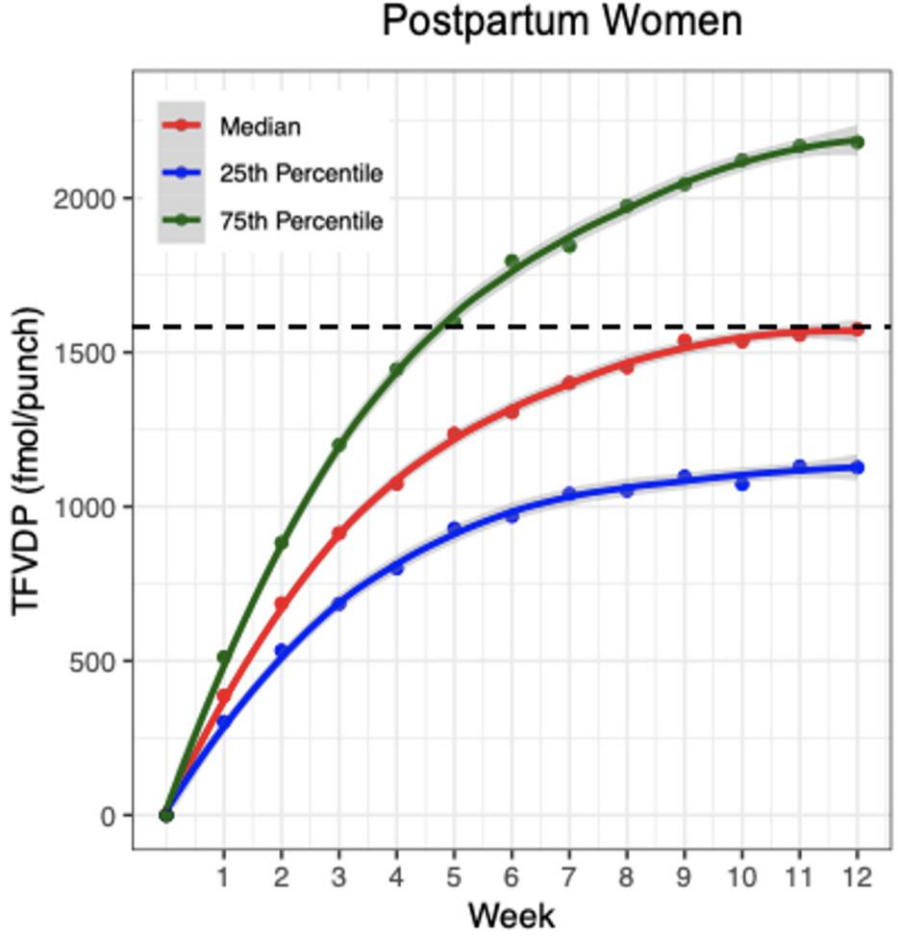
Characterized TFV-DP concentrations in DBS among pregnant and postpartum women under optimal adherence conditions

Sample size: 40

Completed accrual in 4 months

PK Component: Summary





~30% reduction in TFV-DP during pregnancy

Anderson, et al., CROI, 2020
Stranix-Chibanda, et al. CID, 2021

PK Component: TFV-DP Benchmarks

Interpretation	Pregnancy	Postpartum
Green Zone Consistent with highest levels of protection	≥ 650	≥ 1050
Yellow Zone Consistent with some but incomplete levels of protection	200-649	300-1049
Red Zone Consistent with low to no levels of protection	<200	<300

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SMC review (2020)

Reviewed PK and safety data

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PrEP Comparison (2021-2023)

Evaluated adherence, maternal safety (including pregnancy outcomes), and infant safety among women on daily oral FTC/TDF for PrEP

Sample size: 350

Completed accrual in 10 months

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PrEP Comparison Component

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Overview

- Parallel cohort design
- Participants ≤ 32 weeks gestation and eligible for PrEP
- Enrolled based on decision to receive PrEP (Cohort 1) or not receive PrEP (Cohort 2) at a 2:1 ratio
- PrEP intention may change during the study:
  - Initially declined PrEP but later wanted to start → Cohort 2/Step 2
  - Started PrEP but decided to stop → No change to Cohort or Step

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- 7 sites across southern and central Africa:
  - Malawi
  - South Africa
  - Uganda
  - Zimbabwe
- Enrolled adolescent girls and young women, 16-24 years of age, without HIV
- Participants (mother-infant-pairs) followed to 6 months postpartum

Study interventions

- **All participants received:**
  - Integrated Next Step Counseling
  - STI management
  - SMS support for ANC/MCH (one-way)
- **Those on daily oral PrEP (FTC/TDF) received:**
  - Scheduled TFV-DP measurement from DBS
  - Structured biofeedback using PK benchmarks
  - SMS support for PrEP adherence (two-way)

Outcome Measures

Maternal Safety

- Grade ≥3 adverse events
- Grade ≥2 lab abnormalities
- Adverse pregnancy outcomes
  - Fetal loss
  - Preterm delivery (<37 wks)
  - Small for gestational age (<10%tile)

Infant Safety

- Infant death
- Grade ≥3 adverse event
- Infant bone mineral content based on DXA
- Infant renal function
- Infant length for age

Adherence

- TFV-DP concentrations in DBS
- PrEP decision-making and adherence (qualitative)

For the safety analyses, comparison made between **any** PrEP exposure (Cohort 1 *and* Cohort 2/Step 2) versus **no** PrEP exposure (Cohort 2/Step 1)

Study Population

Baseline Characteristics	**Cohort 1** (n=229)	**Cohort 2** (n=121)
Age, median (IQR)	21 (19, 22)	21 (20, 22)
First pregnancy, %	156 (68%)	64 (53%)
Gestational age, weeks median (IQR)	24 (20, 27)	25 (21, 27)
Unemployed, %	188 (85%)	98 (82%)
Perceived risk of getting HIV, %		
No or small chance	110 (51%)	61 (53%)
Moderate or high chance	48 (23%)	25 (22%)
Not sure	55 (26%)	29 (25%)
Primary partnership <12 months	78 (41%)	38 (40%)
Country of enrollment		
Malawi	23 (10%)	27 (22%)
South Africa	29 (13%)	11 (9%)
Uganda	54 (24%)	23 (19%)
Zimbabwe	123 (54%)	60 (50%)

Study completion

Cohort 1:
202 of 229 (88%)

Cohort 2/Step 2:
13 of 13 (100%)

Cohort 2/Step 1:
95 of 108 (88%)

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Results: Maternal Adverse Events

Adverse Events	Any PrEP exposure (Cohort 1 and Cohort 2/Step 2) GRADE 3	4	5	All	No PrEP exposure (Cohort 2/Step 1) GRADE 3	4	5	All
Overall	**27 (11%)**	**3 (1%)**	**1 (<1%)**	**31 (13%)**	**4 (3%)**	**1 (<1%)**	**0 (0%)**	**5 (4%)**
Blood and lymphatic system disorders	1	1	0	2	0	0	0	0
Endocrine disorders	1	0	0	1	0	0	0	0
Gastrointestinal disorders	1	0	1	2	0	0	0	0
Infections and infestations	6	0	1	7	0	0	0	0
Injury, poisoning and procedural complications	0	0	0	0	1	0	0	1
Investigations	3	0	0	3	0	1	0	1
Pregnancy, puerperium and perinatal conditions	20	2	0	22	4	0	0	4
Renal and urinary disorders	1	0	0	1	0	0	0	0
Vascular disorders	1	0	0	1	0	0	0	0

Incidence rates (95%CI) for Grade ≥3 AEs and Grade ≥2 lab abnormalities:

– Any PrEP exposure: 29.4 (22.1, 39.0)
– No PrEP exposure: 18.2 (11.0, 30.2)

Any PrEP vs. no PrEP exposure
Incidence Rate Ratio: 1.62 (0.89, 2.94)

No cases of maternal HIV acquisition

Results: Pregnancy Outcomes

	Any PrEP Exposure (Cohort 1 and Cohort 2/Step 2)	No PrEP Exposure (Cohort 2/Step 1)
Total with delivery information	N= 223	N=112
Any adverse pregnancy outcome	51 (24%)	28 (26%)
Stillbirth/Spontaneous abortion	2 (1%)	4 (4%)
Total with livebirth	N=221	N=108
Pre-term delivery (<37 weeks)	19 (9%)	7 (6%)
Small for gestational age	34 (16%)	19 (18%)

Any PrEP vs. no PrEP exposure

Odds Ratio: 0.88 (0.52, 1.50)

Chi, et al., CROI, 2024

Results: Infant Adverse Events

Adverse Events	Any PrEP exposure (Cohort 1 and Cohort 2/Step 2) GRADE 3	4	5	All	No PrEP exposure (Cohort 2/Step 1) GRADE 3	4	5	All
Overall	**46 (20%)**	**3 (1%)**	**9 (4%)**	**58 (25%)**	**17 (16%)**	**0 (0%)**	**5 (5%)**	**22 (20%)**
Blood and lymphatic system disorders	1	0	0	1	0	0	0	0
Congenital, familial and genetic disorders	0	0	1	1	0	0	0	0
Gastrointestinal disorders	1	0	0	1	0	0	0	0
General disorders and administration site conditions	0	1	0	1	0	0	2	2
Infections and infestations	5	0	4	9	3	0	2	5
Investigations	3	3	0	6	1	0	0	1
Metabolism and nutrition disorders	38	1	0	39	11	0	0	11
Pregnancy, puerperium and perinatal conditions	5	0	0	5	3	0	1	4
Respiratory, thoracic and mediastinal disorders	5	0	4	9	1	0	0	1

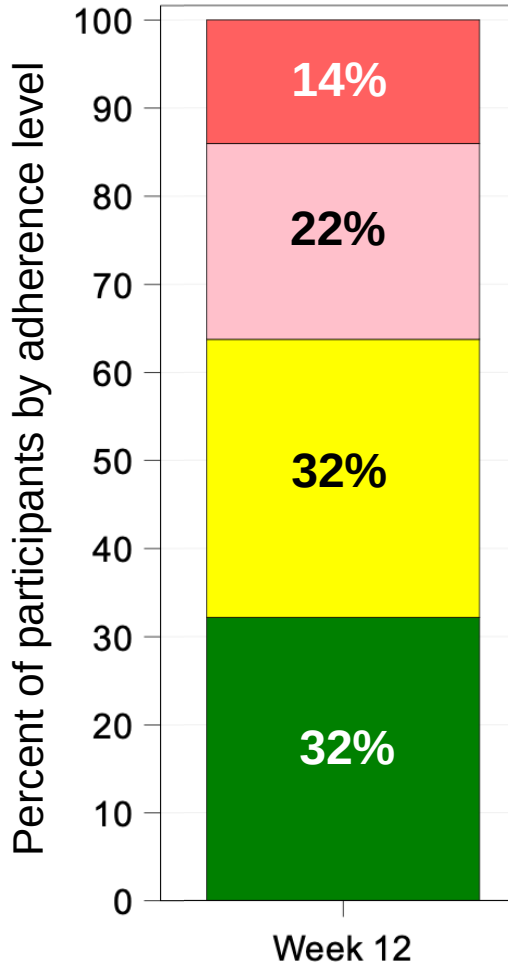
Incidence rates (95%CI) for Grade ≥3 AEs:

– Any PrEP exposure: 42.6 (29.6, 61.2)
– No PrEP exposure: 33.1 (18.4, 59.7)

Any PrEP vs. no PrEP exposure
Incidence Rate Ratio: 1.29 (0.70, 2.38)

Infant growth and DXA analyses underway

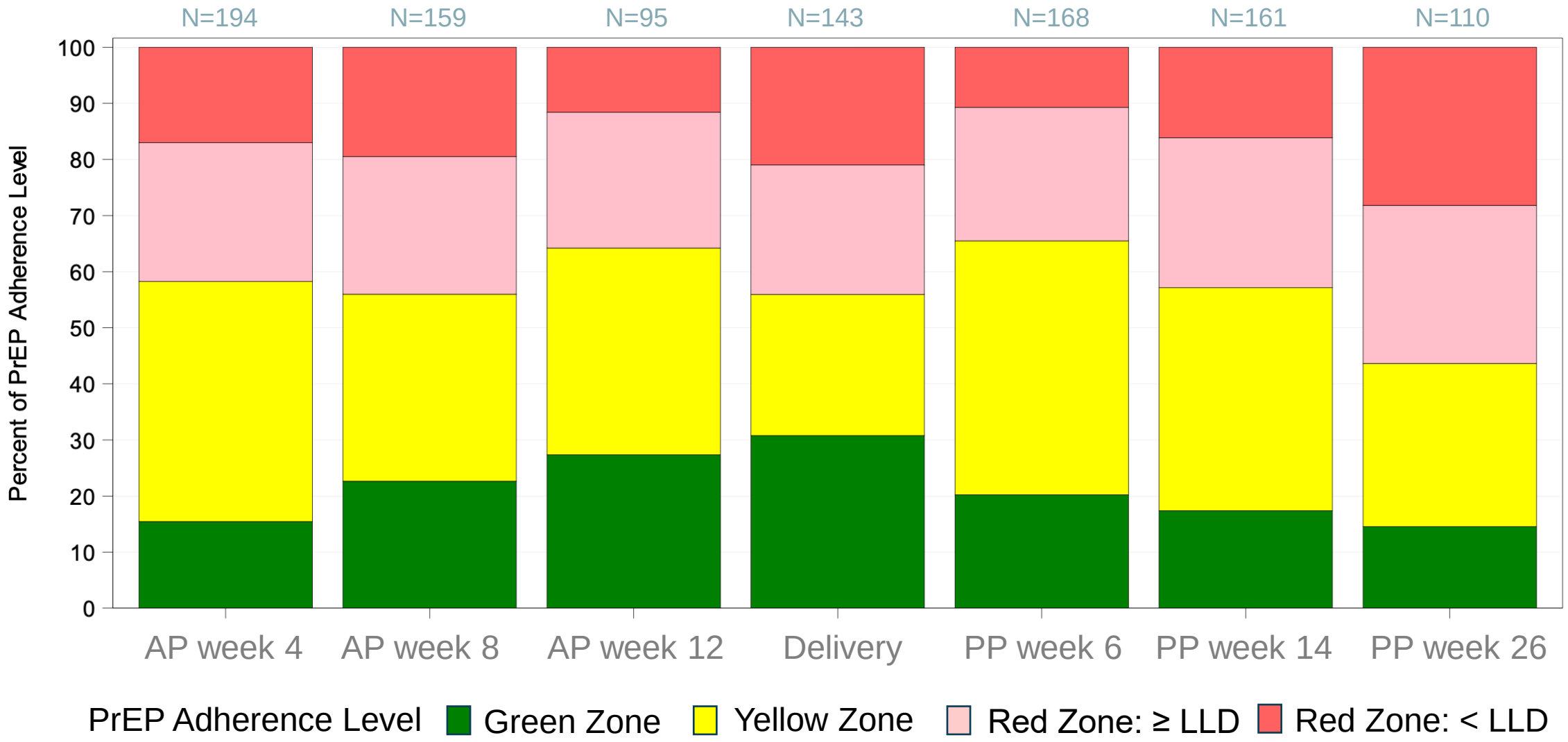
Results: Adherence at 12 Weeks



Among 171 participants with TFV-DP levels at 12 weeks, approximately one-third had concentrations in the highest range

PrEP Adherence Level Green Zone Yellow Zone Red Zone: ≥ LLD Red Zone: < LLD

Results: Adherence over Time



Qualitative In-depth Interviews

Interviewees: 40 initiated PrEP (20 high adherence, 20 low adherence) and 20 declined PrEP

Divided equally among antepartum and postpartum participants

What factors influence decisions about PrEP initiation?

- Perceived risk for HIV
- Prevention methods used
- Reasons for joining the study
- Familiarity with PrEP prior to study

What recommendations do women have for PrEP in pregnancy?

- Facilitators
- Challenges
- Recommendations

What are women's PrEP plans post-study?

- Plans for continuing with PrEP
- Situations where you would want PrEP

Conclusion

- IMPAACT 2009 provides a wealth of data about PrEP use during pregnancy and postpartum
- Daily oral FTC/TDF is safe for mothers and infants
- PrEP use was high but dynamic over time
- Decisions around PrEP rely on contextual factors, including perceived costs and benefits
- Lessons from this study will inform broader implementation strategies for HIV prevention in pregnancy and postpartum

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Qualitative Team: Petina Musara, Juliane Etima, Loveness Imaan, Doreen Kemigisha, Florence Mathebula, Maddy Ligon, Peter Slutzker

Statistical and Data Management Center: Sharon Huang, Deb Kacanek, Benjamin Johnston, Becky Dirschberger, Fred Bone

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Protocol Co-Chairs: Benjamin Chi and Lynda Stranix-Chibanda

Protocol Vice Chair: Rivet Amico

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