Infant safety following exposure to maternal TDF/FTC for HIV prevention in utero and through breastmilk:

IMPAACT 2009

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No conflict of interest

Background

- Daily oral PrEP with tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) is an important component of HIV prevention for pregnant and postpartum populations.
  - No safety concerns from mother or pregnancy outcomes *
  - Reassuring safety regarding infant TDF exposure in utero and through breastfeeding
- IMPAACT 2009 investigated the safety, adherence, and pharmacokinetics of daily oral PrEP during pregnancy and postpartum
- However, TDF exposure may affect infant outcomes, including bone formation, kidney function and growth.
- We evaluated and compared incidence of infant adverse events following in-utero exposure to oral PrEP TDF/FTC among PrEp-exposed and PrEP-unexposed newborns

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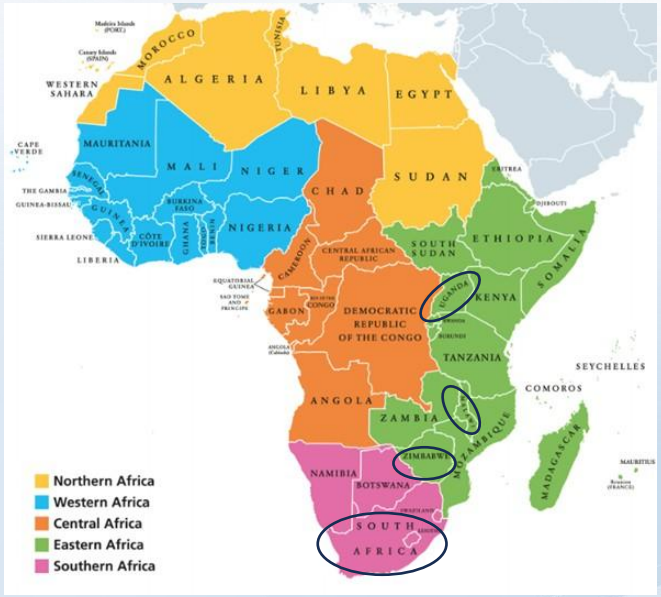
Methods: Study Design

- IMPAACT 2009 enrolled pregnant HIV negative individuals aged 16-24 years, who were eligible for PrEP in four African countries
- Participants opted to initiate (Cohort 1) or decline (Cohort 2) oral PrEP TDF/FTC at enrolment and could change throughout follow-up.
- Infant visits occurred at birth, and weeks 6, 14 and 26.
- Infant adverse events (AEs) were defined as infant death or grade 3 or higher AEs between birth and 26 weeks visit using the NIAID DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events Corrected Version 2.1 July 2017
- Other infant outcomes at birth and 26 weeks included:
  - Bone mineral content (BMC) via dual-energy X-ray absorptiometry (DXA)
  - Creatinine clearance by modified Schwartz criteria
  - Length-for-age z-scores (LAZ) at birth and week 26.
- Exposure defined as any maternal prescription of PrEP TDF/FTC at enrolment or during follow-up.



Methods: Statistical Analysis

- Incidence rates for infant AEs among PrEP-exposed vs PrEP unexposed infants calculated; The unadjusted incidence rate ratio of cumulative adverse events up to the age 26-week visit (among PrEP exposed vs. PrEP unexposed infants) was estimated based on a Poisson distribution with 95% Wald confidence intervals (CI).
- Differences in mean infant growth and development outcomes at birth and age 26 weeks among PrEP exposed and PrEP unexposed infants were calculated. Means were estimated and compared between PrEP-exposed and PrEP unexposed infants using two sample t-tests at each time point.

Results: Infant Demographics

- A total of 350 women enrolled (N=229 in Cohort 1 and N=121 in Cohort 2); 329 pregnancies of women on study at delivery resulted in a live birth.
- All 329 liveborn infants were included in this analysis
  - 230 were PrEP-exposed
  - 99 were PrEP-unexposed
- Cohort 1 group had a higher proportion of males and higher median birth weight
- Otherwise, birth characteristics appeared similar.

		Cohort 1 PrEP exposed N=217	Cohort 2 PrEP unexposed N=112
Sex	Female	97 (45%)	63 (56%)
	Male	**118 (55%)**	**49 (44%)**
	Missing	2	0
Birth weight	**Median (Q1, Q3)**	**3100 (2800,3400)**	**3000 (2740,3300)**

*Mothers of 13/112 Cohort 2 infants switched to PrEP at follow-up (n=4 during antepartum period; n=9 postpartum)

Infant Adverse Events

- Overall incidence of Grade 3 or higher infant adverse events:
  - PrEP-exposed: **66.3** per 100 person years, 95%CI: 45.8, 95.9
  - PrEP-unexposed: **51.7** per 100 person years, 95%CI: 28.4, 94.1
  - Incident rate ratio: **1.28**, 95% CI: 0.63, 2.59
- Most frequently reported AEs: nutrition disorders (mostly underweight), infections, respiratory conditions, and perinatal conditions.
- No AEs were assessed as PrEP-related
- Nine deaths among PrEP-exposed infants and five deaths among PrEP-unexposed infants. No deaths were deemed to be PrEP-related.

Infant Bone Mineral Content, Creatinine Clearance and Growth

			PrEP-exposed	PrEP-unexposed	P value
Lumbar spine BMC (g)	Week 26	Mean (s.d.)	**3.2 (0.6)**	**3.1 (0.7)**	
		Median (Q1,Q3)	3.3 (2.9, 3.6)	3.1 (2.6, 3.4)	
		T-test			0.12
Creatinine clearance (mL/min)	Week 26	Mean	**143.3 (42.5)**	**140.1 (37.3)**	
		Median (Q1,Q3)	140.4 (122.7, 150.0)	135.7 (125.6, 146.3)	
		T-test			0.52
Length for age Z score	Week 26	Mean	**-0.6 (1.2)**	**-0.8 (1.1)**	
		Median (Q1,Q3)	-0.6 (-1.3, 0.2)	-0.7 (-1.7, -0.1)	
		T-test			**0.06**

Conclusion

- Adverse events were more frequently reported for infants with prior PrEP exposure.
- Bone mineral density, renal function, and growth appeared similar between the two groups.
- Overall, infant safety data were reassuring in this rigorous clinical trial
- Daily oral PrEP TDF/FTC remains a safe and important option for HIV prevention during pregnancy and postpartum, especially where risk of HIV exposure is high.

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- Any Questions welcomed ?