TFV-DP in DBS for pregnant/postpartum adolescent and young women on PrEP in Africa

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BACKGROUND

- The risk of HIV acquisition more than doubles in pregnant and postpartum women in sub-Saharan Africa, emphasizing the need for programmatic delivery of HIV prevention services including PrEP.
- Intracellular tenofovir-diphosphate (TFV-DP) in red blood cells measured with dried blood spots (DBS) is an established biomarker of cumulative PrEP adherence given its 17 day half-life, analogous to HbA1C for diabetes.
- TFV-DP in DBS informs adherence-efficacy relationships for PrEP. This has been defined for men who have sex with men, but not for pregnant or non-pregnant women.
- Pregnancy causes physiological changes expected to lower TFV-DP in DBS including increased TFV renal clearance and hemodilution.
- IMPAACT 2009 is a two-component observational trial in pregnant and postpartum adolescent girls and young women in sub-Saharan Africa. This communication presents results from the first (PK) component.

OBJECTIVES

The goal of the IMPAACT 2009 PK component was to establish adherence benchmarks for TFV-DP in DBS for pregnant and postpartum adolescents and young women who took PrEP daily under direct observation, and to compare these benchmarks in the pregnant and postpartum groups.

METHODS

- HIV-negative adolescent girls and young women (16-24 years) were recruited in Malawi, South Africa, Uganda, and Zimbabwe
  - Pregnant: 14-24 wks gestation at enrollment
  - Postpartum: 6-12 wks postpartum at enrollment
- Daily FTC/TDF was administered for 12 weeks under direct observation (in person or by live video streaming).
- Five 50uL DBS were collected weekly and stored at -80°C.
- TFV-DP was assayed in one 50uL spot by validated LC-MS/MS at the University of Cape Town and reported as fmol/3mm punch for consistency with previous studies.
- Summary statistics were used for observed data at week 12.
- A one-compartment IV infusion non-linear mixed effects model was fit to concentration time data for individual predictions (modeled data).
- Observed TFV-DP at week 12 was compared between the pregnant and postpartum groups with the Wilcoxon test.

RESULTS

- 20 pregnant and 20 postpartum women enrolled between March-May 2019
- 3348 of 3360 (>99%) total doses were directly observed
- All participants met criteria for inclusion in the analysis

Adherence benchmarks using TFV-DP in DBS were established for pregnant/postpartum African adolescents and young women

TFV-DP in DBS was 31%-37% lower in pregnancy compared with postpartum, in line with expectations. Strict adherence to PrEP is recommended during pregnancy.

Table 1. Baseline Demographics

Characteristic	Pregnant (N=20) median (IQR)	Postpartum (N=20) median (IQR)
Age (yrs)	20 (19.5, 22.5)	20 (19, 22)
Weight (kg)	59 (56, 65)	55 (51, 62)
HCT (%)	34.9 (33, 37.1)	40.8 (39.1, 41.7)
CLcr (CG-ideal wt; ml/min)	151 (130, 169)	109 (102, 123)
Gestational Age (wks)	18 (15, 20)	NA
Postpartum (wks)	NA	7 (7, 9)

Table 2. TFV-DP at Week 12 Visit

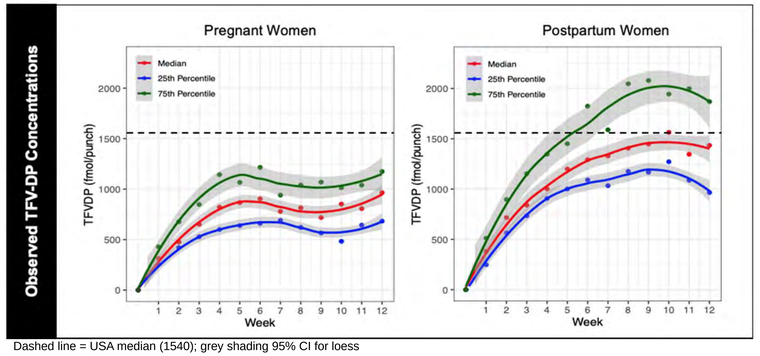
Characteristic	Pregnant (N=20) median (IQR)	Postpartum (N=20)* median (IQR)	Difference (p Wilcoxon)
Observed TFV-DP (fmol/punch)	965 (691, 1166)	1406 (1053, 1859)	31% (p=0.0064)
Modeled TFV-DP (fmol/punch)	890 (704, 1143)	1418 (1179, 2139)	37% (p<0.0001)
Modeled T-1/2 (days)	14 (10.6, 17.6)	16.5 (13.7, 21.2)	ND

One week 12 value was missing, and their concentration at week 11 was used. Median IQR was 1434 (966, 1869) if only week 12 was used.

- Figures 1 and 2 show TFV-DP concentration time profiles for observed (Figure 1) and modeled (Figure 2) data.
- Figure 3 shows estimated thresholds. These were based on 25th percentiles of observed data that were rounded down to establish the highest adherence group. Lower adherence categories were determined assuming dose-proportionality.

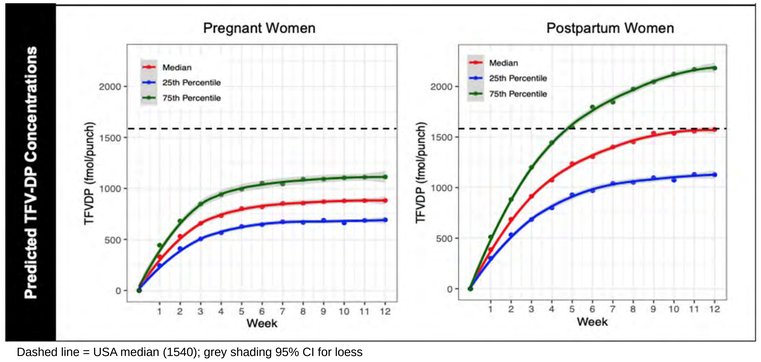
RESULTS

Figure 1. Observed TFV-DP



Dashed line = USA median (1540); grey shading 95% CI for loess

Figure 2. Modeled TFV-DP



Dashed line = USA median (1540); grey shading 95% CI for loess

CONCLUSIONS

- Adherence benchmarks were established for TFV-DP in DBS for pregnant and postpartum adolescents and young women (Figure 3, right).
- TFV-DP in DBS was 31%-37% lower in pregnant compared with postpartum women, in parallel with increased renal function and lower HCT. This is consistent with prior studies.
- Strict PrEP adherence is recommended during pregnancy. Future studies can use these adherence benchmarks to support PrEP adherence and determine adherence-efficacy relationships.

Figure 3. Proposed thresholds

	DBS TFV-DP fmol/punch	
Interpretation	Pregnant	Post-partum
~7 doses/wk	≥650	≥950
2–6 doses/wk	200–649	250-949
<2 doses/wk	<200	<250

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