Exploring Long-Term Adherence Markers Using Hair and Dried Blood Spots in iPrEX OLE

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BACKGROUND

- Efficacy of tenofovir (TFV) disoproxil fumarate (TDF)/ emtricitabine (FTC)-based PrEP dependent on adherence
- Limitations of self-report/pill counts in predicting seroconversions in PrEP trials have led to interest in pharmacologic measures of adherence (drug levels)
- Substantial discordance between self-reported measures of adherence and drug detection in PrEP trials e.g. global iPrEx[1,2], Partners PrEP[3,4], FEM-PrEP[5], and VOICE[6]
- TFV or TFV-diphophate (TFV-DP) levels in plasma, PBMCs, and dried blood spots (DBS) strongly predictive of protective efficacy in iPrEX[1] or iPrEX OLE[7]
- Drug levels in plasma, PBMCs represent shorter-term exposure than concentrations in DBS and hair samples[8]
- Hair samples to measure PrEP adherence/exposure have additional advantage of avoiding cold chain (can be stored and shipped at room temperature without biohazard)
- This study assesses correlation between PrEP drug concentrations in DBS and hair samples for first time

METHODS

- **Study population:** iPrEx Open Label Extension (OLE) enrolled 1603 HIV-negative MSM and transwomen; 1225 initiated PrEP
- **DBS and hair collection/measurement:**
  - Visits performed at baseline and weeks 4, 8, 12, 24, 36, 48, 60 and 72.
  - Whole blood collected for DBS prep routinely 4 and 8 weeks after PrEP initiation, then every 12 weeks
  - Hair samples collected from consenting participants on opt-in basis every 12 weeks
  - Hair levels of TFV/FTC and DBS levels of TFV-DP and FTC-triphosphate (FTC-TP) measured via liquid chromatography/tandem mass spectrometry
- **Statistical analysis:** Spearman's correlation coefficients and scatterplots assessed relationships between TFV and FTC levels in hair and TFV-DP and FTC-TP concentrations in red blood cells measured with DBS. Concordance of drug detection determined for paired samples.

RESULTS

- Drug levels from **806** paired hair-DBS samples (217 participants) available for comparison
- TFV or FTC hair concentrations and TFV-DP or FTC-TP levels in DBS strongly correlated (**Figure 1**)
- Drug detectability in two matrices mostly concordant (**Table 1**)

RESULTS

Figure 1: Scatterplots showing correlations between A) TFV concentrations in hair with TFV-DP levels in DBS; B) TFV levels in hair with FTC-TP levels in DBS; C) FTC levels in hair with FTC-TP levels in DBS; D) FTC levels in hair with TFV-DP levels in DBS

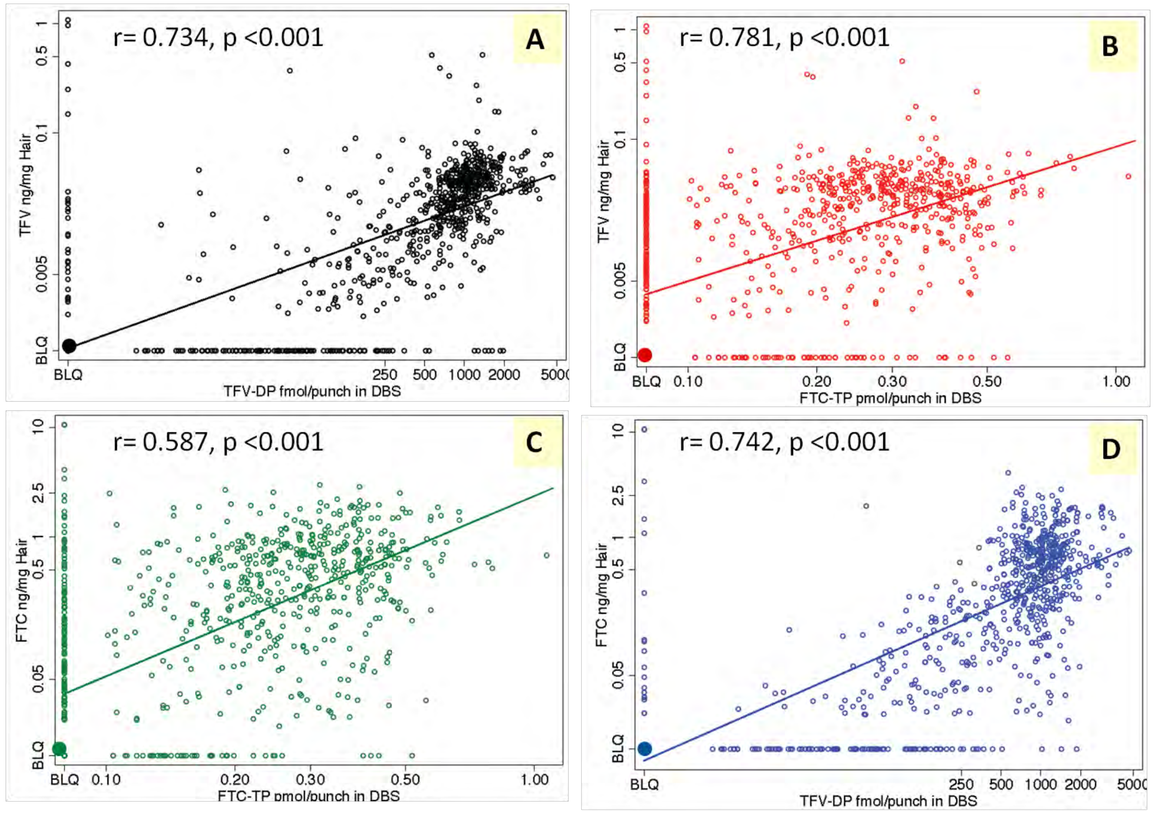


Table 1: Comparison of levels of detection of PrEP drugs in hair and DBS. 806 paired samples

Drug level, matrix	Detectable in hair and DBS (%)	Detectable in hair, not DBS (%)	Detectable in DBS, not hair (%)	Undetectable in both matrices (%)	Drug detection concordant in both matrices
TFV level in hair, TFV-DP in DBS	72%	3%	15%	10%	**82%**
TFV level in hair, FTC-TP in DBS	71%	5%	5%	19%	**90%**
FTC level in hair, FTC-TP in DBS	62%	14%	5%	19%	**81%**
FTC level in hair, TFV-DP in DBS	74%	2%	13%	11%	**85%**

DISCUSSION/CONCLUSION

- Objective pharmacologic measures of drug exposure have been crucial for trial interpretation in several PrEP studies[1,2,5,6]
- Emerging interest in incorporating feasible measures of exposure in real-life PrEP settings
- DBS and hair both have feasibility advantages and hair samples do not require a cold chain or biohazard precautions for storage and shipment
- This study shows strong and significant correlations between concentrations of PrEP drugs in hair and DBS, as well as high concordance (>80% for all combinations) for drug detectability in the two matrices
- Only 28 on-PrEP seroconversions in iPrEx OLE; not enough hair from relevant visits to perform meaningful analysis between hair levels of drug and protective efficacy (12 declined or didn't have enough hair; 6 had hair collected but only at HIV RNA negative timepoints; only 10 had hair collected at HIV RNA+ timepoints)
- Drug levels in DBS predict protective efficacy in iPrEx OLE[7]; strong correlation between hair and DBS levels suggest hair concentrations could be predictive
- Further study examining protective efficacy of hair concentrations of TFV/FTC in PrEP needed

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