URINE TENOFOVIR LEVELS BY IMMUNOASSAY PREDICT HIV PROTECTION IN A LARGE PrEP TRIAL

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BACKGROUND

Existing biomarkers of PrEP adherence are limited by:

- High cost of assays
- Need to often ship samples offsite for analysis
- Need for specialized laboratory equipment and trained personnel

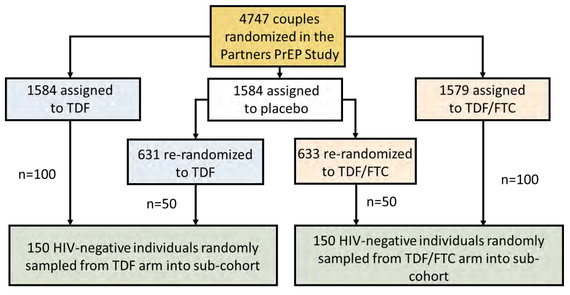
We developed a novel immunoassay that detects tenofovir (TFV) in urine within minutes, for eventual use at the point of care (POC)

OBJECTIVES

1. Compare urine TFV measurements by enzyme-linked immunoassay (ELISA) to TFV levels in plasma
2. Evaluate the ability of the immunoassay to predict HIV protection

METHODS

Participants: Sub-cohort of PrEP users in HIV serodiscordant couples (figure below) and HIV seroconverters from the Partners PrEP Study



***TFV measurement*:** Stored urine was analyzed by ELISA; date-matched plasma was analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS)

Analysis:

1. Calculated sensitivity and specificity of detectable urine TFV levels (≥ assay lower limit of quantification [LLOQ] of 1000 ng/mL) for detecting any plasma TFV (≥ LC-MS/MS LLOQ of 0.31 ng/mL)
2. Assessed whether urine TFV ≥1500 (a cutoff associated with PrEP dosing in the past day in a directly-observed therapy study) was predictive of HIV protection using a nested case-control design
   - *Case samples*: Collected at the visit of first HIV detection
   - *Control samples*: From participants who were HIV-negative at case HIV detection; matched 35:1 using risk set sampling
   - Rate ratios (RR) estimated using conditional logistic regression adjusting for age, sex, report of condomless sex at enrollment

A novel urine tenofovir test showing recent PrEP adherence predicts a ***71% HIV risk reduction*** *among participants in a large PrEP trial.*

RESULTS

292/300 individuals in the sub-cohort had an available urine sample
- 39% were female
- median age: 33 (IQR: 28-39)

22/52 cases had an available urine sample
- 55% were female
- median age: 33 (IQR: 27-39)

Sensitivity & specificity for detecting plasma TFV

	Detectable Plasma TFV	Undetectable Plasma TFV
Detectable Urine TFV	486	45
Undetectable Urine TFV	72	119

Lower limit of quantification in plasma with LC-MS/MS: 0.31 ng/mL
Lower limit of quantification in urine with ELISA: 1000 ng/mL

Sensitivity: 486/558 (87%, 95% CI: 84-90%)
Specificity: 119/164 (73%, 95% CI: 65-79%)

HIV risk reduction associated with urine TFV ≥1500 ng/mL

Case samples TFV ≥1500 ng/mL, n (%)	Control samples TFV ≥1500 ng/mL, n (%)	% risk reduction (95% CI)	Adjusted % risk reduction (95% CI)
8/22 (36%)	527/770 (68%)	73% (36 - 89%)	71% (30 - 88%)

TFV=tenofovir, CI=confidence interval; % risk reduction= (1-RR)*100; [a]Adjusted for sex, age at enrollment, and report of any condomless sex with study partner in past month at enrollment

CONCLUSIONS

- The novel urine TFV immunoassay was predictive of HIV protection in a large completed PrEP trial and had good sensitivity and specificity for TFV detection in plasma
- The assay could be a valuable tool for facilitating real-time feedback of PrEP use to both provider and patient, allowing for immediate adherence intervention

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