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Point-of-Care Urine Tenofovir Testing to Detect HIV Drug Resistance

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Background

- Point-of-care urine tenofovir (TFV) assays have been developed and validated in laboratory settings
- However, their utility as a clinical tool to help determine the cause of virologic failure remains untested

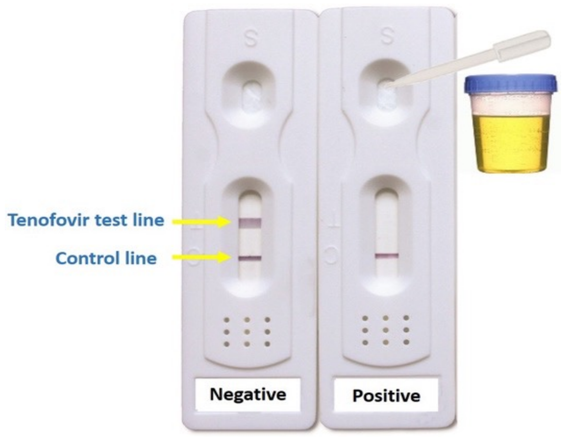
Objective: Evaluate a point-of-care (POC) urine tenofovir (TFV) assay to indicate HIV drug resistance (HIVDR) for patients failing first-line ART.

Methods

- **Study Design:** Diagnostic validity assessment using specimens collected during the REVAMP clinical trial[1]
- **REVAMP Study Setting:** Public-sector clinics in Durban, South Africa and Mbarara, Uganda
- **REVAMP Study Population:** Adults ≥ 18y with virologic failure on NNRTI-based first-line ART
- **REVAMP Study Procedures:**
  - Blood and urine collected at each study visit
  - Blood tested for viral load (VL) and HIVDR if >1000 copies/mL
  - Urine tested with POC lateral flow assay (**Figure 1**)
- **Inclusion Criteria for Analysis:**
  - On TFV-containing ART regimen
  - Paired urine and HIVDR results available
- **Predictor of interest:** ART adherence as determined by presence of TFV on urine POC lateral flow assay
- **Outcome of interest:** HIV drug resistance defined as intermediate to high-level resistance to any drug in the current ART regimen (Stanford algorithm)
- **Statistical Analyses:** Calculated test performance characteristics of POC urine TFV assay to detect HIVDR

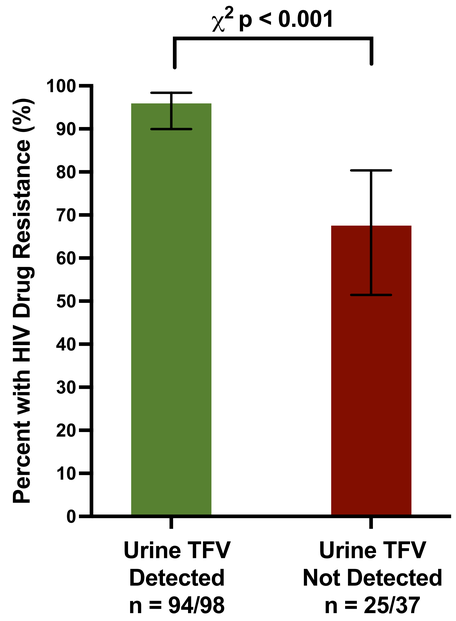
In a setting with a high prevalence of HIV drug resistance, **the point of care urine tenofovir assay had a positive predictive value of 96% to detect HIV drug resistance.**

Figure 1. Point-of-Care Urine Tenofovir Assay[2]



- Cutoff value for detection of TFV: 1,500 ng/mL
- Validated against liquid chromatography tandem mass spectrometry

Figure 2. Proportion with HIVDR in Participants with and without Detectable Urine TFV



Study Population Characteristics

n = 135	
Female, n (%)	59 (44)
Age (years), median (IQR)	38 (31 – 44)
Years on ART, median (IQR)	4.4 (3.5 – 6.8)

Urine Tenofovir Test Performance Characteristics to Detect HIVDR

Sensitivity	79%
Specificity	75%
Positive Predictive Value	96%
Negative Predictive Value	32%
Observed HIVDR Prevalence	*88%*

Expected Positive and Negative Predictive Values Across Varied Prevalence of HIVDR

Estimated HIVDR Prevalence	Positive Predictive Value	Negative Predictive Value
90%	97%	28%
75%	90%	54%
50%	76%	78%
25%	51%	91%
10%	26%	97%

Conclusions

- POC urine assay had a PPV of 96% to detect HIVDR in this population (observed HIVDR of 88%)
- The assay would also have a high NPV in settings where HIVDR prevalence is low (<10%)
- In both scenarios, the POC urine TFV assay could:
  - Provide a novel, low-cost method to confirm or exclude HIVDR
  - Inform clinical care and the need to switch to second-line ART
- Future work should assess its utility in real time

References

1. Siedner MJ, et al. Resistance testing for management of HIV virologic failure in sub-Saharan Africa: an unblinded randomized controlled trial. *Ann Intern Med*. 2021 Oct 26; PMID: 34698502
2. Gandhi M, et al. Development and validation of the first point-of-care assay to objectively monitor adherence to HIV treatment and prevention in real-time in routine settings. *AIDS*. 2020 Feb 1;34(2):255–260. PMCID: PMC7021226

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