



A Point-of-Care Urine Tenofovir Adherence Feedback Intervention Improved PrEP Adherence among Kenyan Women

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Discontinuation, suboptimal adherence, and reinitiation of oral HIV pre-exposure prophylaxis: a global systematic review and meta-analysis

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THE LANCET
HIV

- Systematic review, 41.0% of those on PrEP discontinued within 6 months; suboptimal adherence for those who stayed 37.7%
- Discontinuation rate higher in sub-Saharan Africa 47.5% than other regions, particularly among women in non-serodiscordant partnerships and among young women
- Discontinuation rates lower in studies with adherence interventions than in those without (24.7% vs 36.7%, $p=0.015$)

Objective measures critical to interpretation of PrEP trials

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- Efficacy of TDF/FTC in iPrEx rose from 44% to an estimated 92% (CI 40, 99%) among those with detectable drug levels (plasma or PBMC)
- Efficacy 93% (CI 60, 99%) Partners PrEP with high tenofovir (TFV) plasma levels

Adherence Measure	VOICE	FEM-PrEP
Self-report	91%	95%
Returned pill counts	92%	88%
Plasma TFV detection	29%	24%

Short-term adherence metrics predictive of PrEP efficacy in major trials

	Efficacy in randomized comparison	% of blood samples with tenofovir detected
Partners PrEP¹	75%	81%
TDF2²	62%	79%
iPrEx³	44%	51%
FEM-PrEP⁴	6%	26%
VOICE	-4%	29%

TFV-DP DBS	n=126 PPV	NPV
Urine	91%	87%
Self-report	75%	88%
OR 30.2, p<0.0001 for urine predicting TFV-DP, Self-report did not add to prediction ⁶		

¹Baeten et al N Engl J Med 2012; ²Thigpen et al N Engl J Med 2012; ³Grant et al N Engl J Med 2010; ⁴Van Damme et al N Engl J Med 2012; ⁵Marrazzo et al NEJM 2015; ⁶Mustanski et al CROI 2023



PrEP Pharmacologic-based feedback

- **Dapivirine ring-** ideal to have real time feedback on adherence using objective measures
- **PATH PrEP-** brief intervention triggered by low plasma TFV improved adherence (pre/post), real-time would be preferable
- **HPTN 082-** Among young African women, DBS Drug concentration triggered SMS did not increase adherence
 - Delays and errors likely limited effectiveness

	Counseling Message
	<p><u>4 or more doses per week (>500 fmol/punch at wk 4 and >700 fmol/punch at wk 8)</u></p> <p>Key message: You are doing great! Keep up the good work and remember that taking one PrEP pill every day is needed for strong protection against HIV.</p>
	<p><u>~1-3 doses per week (between detectable – 499 fmol/punch at wk 4 and detectable to 699 fmol/punch at wk 8)</u></p> <p>Key message: It looks like you are trying to take the PrEP medication, but are having some difficulties. Remember that taking one pill every day is needed for strong protection against HIV. How can we help you do even better?</p>
	<p><u>No TFV-DP detected (below quantification of 16.6 fmol/punch)</u></p> <p>Key message: It looks like you haven't been able to take the PrEP medication. Is PrEP something that you are still interested in? If yes, how can we help you?</p>

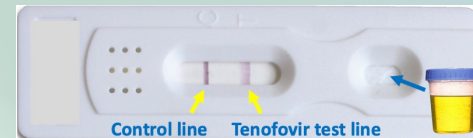


Development of a Point-of-Care Urine Assay for Tenofovir

- Immunoassay for urine tenofovir (TFV) using highly selective antibody developed & validated¹⁻³ as objective adherence metric

Highly (97-99%) sensitive & specific when compared to gold standard liquid chromatography tandem mass spectrometry⁴ (R^2 0.92; $p < 0.001$)

- Immunoassay is now a **POC lateral flow assay**
 - Real-time yes/no answer re TFV ingestion in last 5d
 - Urine TFV cut-off = **1500 ng/ml**
 - Results in 3 Minutes



¹Gandhi M, et al. AIDS 2020. PMID 31634188; ²Gandhi M, et al. JAIDS 2019. PMID 30664078; ³Gandhi M, et al. EClinicalMedicine 2018. PMID 30906930; ⁴Spinelli et al. Curr HIV/AIDS Rep 2020. PMID 32424549

Urine tenofovir test predicts seroconversion in large PrEP trials (Partners PrEP, iPrEx OLE)

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Clinical Infectious Diseases

BRIEF REPORT

Urine Tenofovir Levels Measured Using a Novel Immunoassay Predict Human Immunodeficiency Virus Protection

Randy M. Stalter,^{1,2} Jared M. Baeten,^{1,2,3} Deborah Donnell,^{1,4} Matthew A. Spinelli,⁵
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Nelly Mugo,^{1,7} Andrew Mujugira,^{1,8} Mark Marzinke,⁹ Craig Hendrix,⁹ and
Matthew A. Spinelli,⁵ for the Partners PrEP Study Group



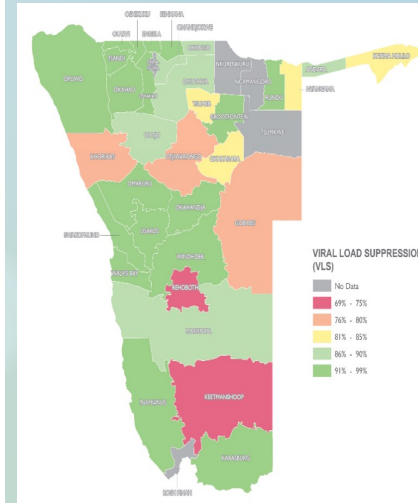
Low tenofovir level in urine by a novel immunoassay is associated with seroconversion in a preexposure prophylaxis demonstration project

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HIV Virologic Suppression Improved after Adherence Intervention Using Urine Assay

- Study in Namibia for patients who do not suppress despite enhanced adherence counseling (EAC) on tenofovir-lamivudine-dolutegravir (TLD)
- Urine test administered in 38 clinics monthly at ART pick-ups
- 200 PLWH enrolled, viral load >1000 despite EAC x >3 months
- Data available to date:
 - **87% (111/127) now virologically suppressed by month 6; $p < 0.001$**
 - **86% of participants and 91% of providers agreed/strongly agreed that the urine test should be in care**
 - **Remarkable as group did not originally suppress after standard WHO counseling**
 - **Only 33% suppress after a standard second EAC session**

Viral Suppression by Region in Namibia

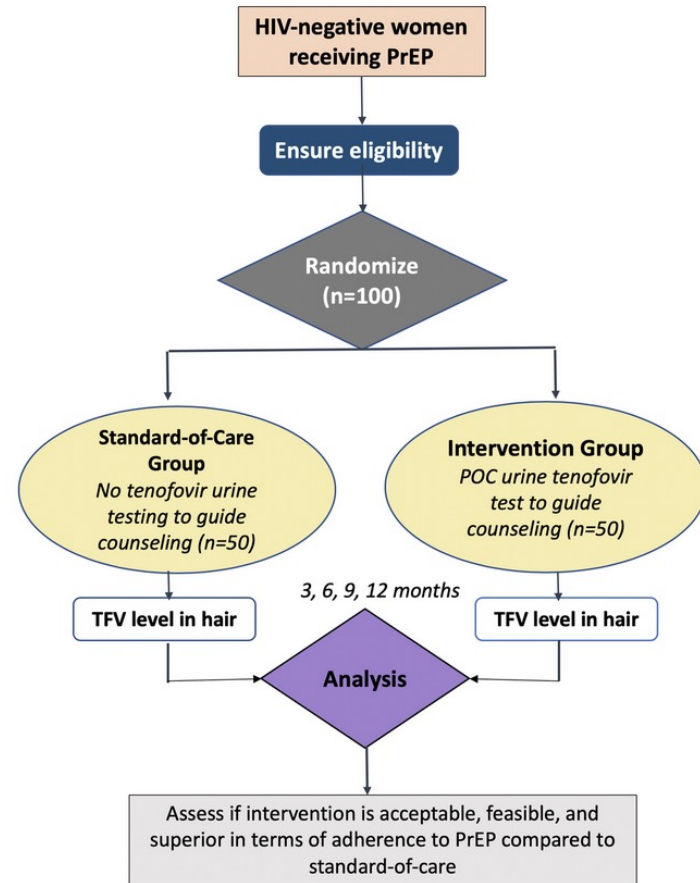


PUMA Study (POC-Urine Monitoring Of Adherence) Study Overview

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- 100 women in non-serodiscordant relationships in Kenya randomized 1:1 to standard PrEP Care or Urine TFV Adherence Feedback
 - Approach informed by IMB model of PrEP Adherence and Motivational Interviewing
- Primary Outcome: Change in TFV Levels in Hair at M12
- Secondary Outcomes: **Urine Adherence Testing** and Acceptability





Drug-Level Feedback Counseling Delivered at Quarterly PrEP Visits

Enrollment and randomization of adherence-challenged participants 3 months after PrEP initiation

N=100 women not
in SDC starting
PrEP in Kenya

N=50
Intervention arm

N=50
Standard of care arm

Feedback on adherence at months
3, 6 and 9: *Intervention arm only*



Months 3, 6, and 9 after
PrEP initiation (Visits 1, 2, 3)

All participants

HIV testing, creatinine, pregnancy testing, self-reported adherence; adherence counseling, PrEP provision

Urine collection



Hair collection



Post-study acceptability
and feasibility surveys

Month 12
(Visit 4, final)

All participants

Urine collection



Hair collection



5
4
3
2
1



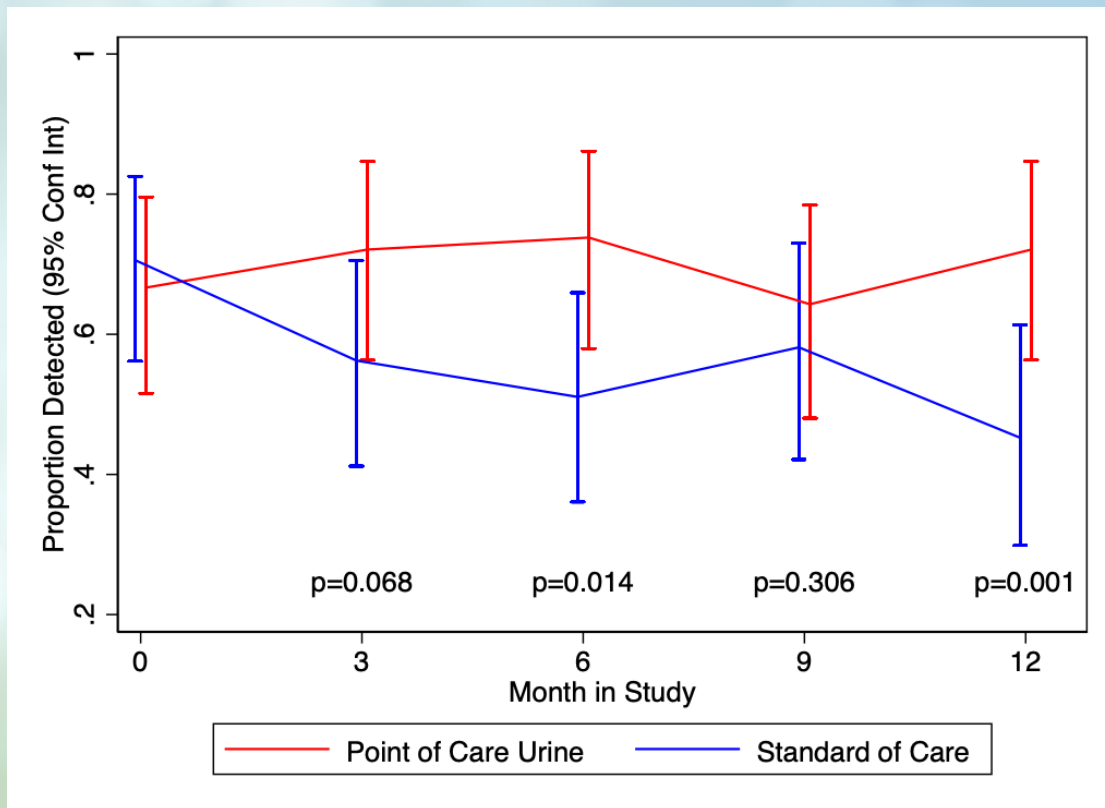
Participant Demographics

Overall (100 Women; 49 Intervention 51 Standard of Care)	
Intervention Dates	3/2021-1/2022
Median Age	34.5 (IQR 25.9-38.6)
Transactional Sex in Prior Month	42%
Self-Reported Adherence	80% Reported Daily Dosing



PUMA Increase Urine Adherence at M12

Visit	Urine POC +	p-value
Baseline	67% vs. 71%	-
Month 3	72% vs. 56%	0.068
Month 6	74% vs. 51%	0.014
Month 9	64% vs. 58%	0.306
Month 12	72% vs. 45%	0.001





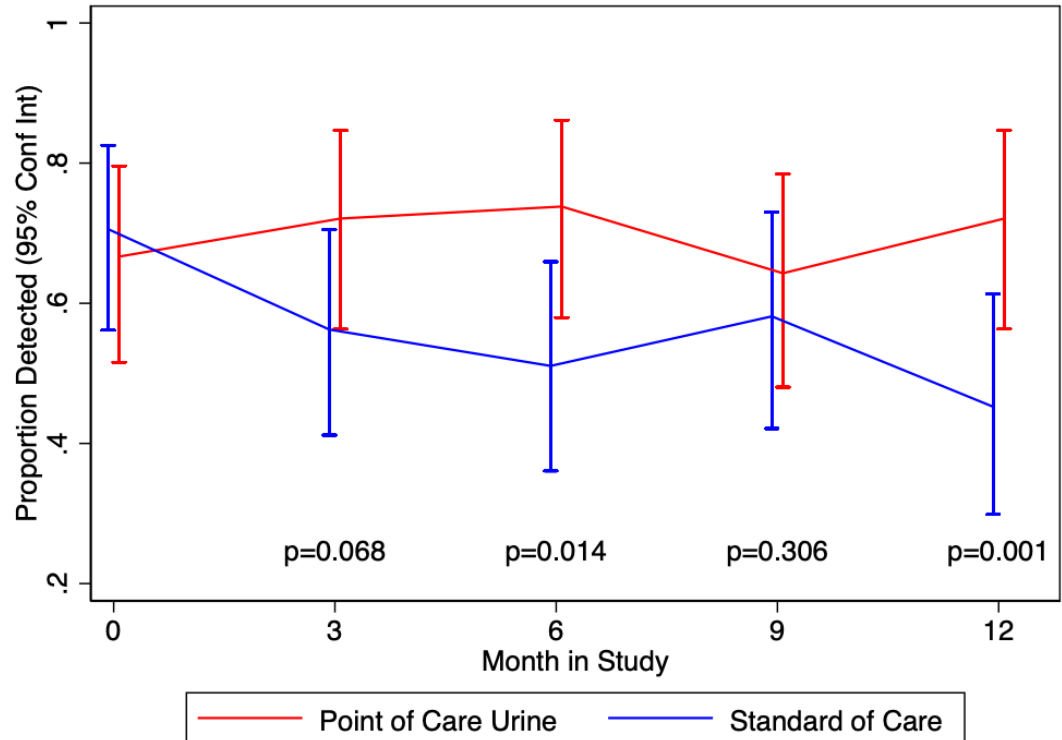
PUMA Increase Urine Adherence at M12

- 20 Interviews Completed

I used to forget taking medication but since they brought this thing of testing (urine assay kit), at least I do not forget, I take the medication daily, since I know I have to be tested (IDI: 24-year-old woman)

- Participants reported less worry of acquiring HIV due to positive urine assay test results.

Another advantage is that even if you have sex with someone you suspect because you have taken those drugs and you are tested, so even if you don't trust the person if you take the drugs, you cannot be infected (IDI: 21-year-old woman)





Conclusions

- PUMA led to higher urine TFV levels at Month 12 in a randomized-controlled trial
- Primary impact appeared to be maintenance of adherence over time, additional interventions may be needed for non-responders targeted by urine test
- Limitation: Cannot exclude “white-coat adherence”
- TFV hair-levels, adherence predictors, and acceptability analyses ongoing and will be available soon



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- Nelly Mugo
- Monica Gandhi
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