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

Jing Zhang*, Chunyan Li*, Junjie Xu*, Zhili Hu, Sarah E Rutstein, Joseph D Tucker, Jason J Ong, Yongjun Jiang, Wenqing Geng, Sarah T Wright,

• 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

- 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

<table>
<thead>
<tr>
<th>Adherence Measure</th>
<th>VOICE</th>
<th>FEM-PrEP</th>
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</thead>
<tbody>
<tr>
<td>Self-report</td>
<td>91%</td>
<td>95%</td>
</tr>
<tr>
<td>Returned pill counts</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Plasma TFV detection</td>
<td>29%</td>
<td>24%</td>
</tr>
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Grant et al. NEJM 2010; Marrazzo et al. NEJM 2015; Van Damme et al. NEJM 2012; Baeten et al. NEJM 2012; Donnell et al. JAIDS 2014
### Short-term adherence metrics predictive of PrEP efficacy in major trials

<table>
<thead>
<tr>
<th></th>
<th>Efficacy in randomized comparison</th>
<th>% of blood samples with tenofovir detected</th>
<th>TFV-DP DBS n=126</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PrEP(^1)</td>
<td>75%</td>
<td>81%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF(^2)</td>
<td>62%</td>
<td>79%</td>
<td></td>
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<tr>
<td>iPrEx(^3)</td>
<td>44%</td>
<td>51%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>FEM-PrEP(^4)</td>
<td>6%</td>
<td>26%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VOICE</td>
<td>-4%</td>
<td>29%</td>
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**TFV-DP DBS**

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>91%</td>
<td>87%</td>
</tr>
<tr>
<td>Self-report</td>
<td>75%</td>
<td>88%</td>
</tr>
</tbody>
</table>

OR 30.2, p<0.0001 for urine predicting TFV-DP, Self-report did not add to prediction\(^6\)

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 preferrable

- **HPTN 082**- Among young African women, DBS Drug concentration triggered SMS did not increase adherence
  - Delays and errors likely limited effectiveness
Development of a Point-of-Care Urine Assay for Tenofovir

- Immunoassay for urine tenofovir (TFV) using highly selective antibody developed & validated\(^1\)\(^-\)\(^3\) as objective adherence metric

Highly (97-99\%) sensitive & specific when compared to gold standard liquid chromatography tandem mass spectrometry\(^4\) \((R^2 0.92; p<0.001)\)

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

Urine tenofovir test predicts seroconversion in large PrEP trials (Partners PrEP, iPrEx OLE)
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
PUMA Study (POC-Urine Monitoring Of Adherence) Study Overview

- 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

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

N=50 Standard of care arm

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
## Participant Demographics

<table>
<thead>
<tr>
<th>Overall (100 Women; 49 Intervention 51 Standard of Care)</th>
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<tbody>
<tr>
<td>Intervention Dates</td>
<td>3/2021-1/2022</td>
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<tr>
<td>Median Age</td>
<td>34.5 (IQR 25.9-38.6)</td>
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<tr>
<td>Transactional Sex in Prior Month</td>
<td>42%</td>
</tr>
<tr>
<td>Self-Reported Adherence</td>
<td>80% Reported Daily Dosing</td>
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# PUMA Increase Urine Adherence at M12

<table>
<thead>
<tr>
<th>Visit</th>
<th>Urine POC +</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>67% vs. 71%</td>
<td>-</td>
</tr>
<tr>
<td>Month 3</td>
<td>72% vs. 56%</td>
<td>0.068</td>
</tr>
<tr>
<td>Month 6</td>
<td>74% vs. 51%</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td>Month 9</td>
<td>64% vs. 58%</td>
<td>0.306</td>
</tr>
<tr>
<td>Month 12</td>
<td>72% vs. 45%</td>
<td><strong>0.001</strong></td>
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</tbody>
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![Graph showing Proportion Detected (95% Conf Int) vs Month in Study with p-values for different months.](image)
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)*

Ngure et al. CROI 2023 #973
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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