

### Adherence 2017

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## Associations Between Urine Tenofovir Levels, Pharmacy Measures, and Self-Report for HIV PreExposure Prophylaxis Adherence Monitoring

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#### Background

- PrEP efficacy is dependent on adherence
- Objective adherence monitoring tools are needed in real-world clinics to help identify potential adherence problems
- Dried blood spot (DBS) testing is the research gold standard
  - Clinical settings often lack access to DBS
- Other strategies include: patient self-report (subjective) and medication possession ratio (MPR) (an objective proxy)
  - MPR = # pills dispensed by pharmacy / days between refills
- Urine tenofovir (TFV) testing is gaining evidence as a noninvasive, inexpensive method for monitoring adherence, that can be collected at the same time as other urine studies
- Self-report and MPR have not been established against urine, but have been compared with DBS and plasma

### Background: Urine Assay

Urine TFV (ng/mL)	Adherence Level	Date Last Dose	Implication	
>1000	Recent	Within 48	HIV protection	
71000	adherence	hours	The protection	
	Low adherence	2-7 days ago	Sub-optimal HIV	
10-1000			protection, at risk of	
			resistance	
<10	Non-adherence	>7 day <mark>s</mark> ago	No HIV protection, low	
< 10			risk of resistance	

#### **STUDY OBJECTIVES:**

- Evaluate the association of 3-Month MPR with urine TFV testing
- Evaluate the association of 7-day self-report with urine TFV testing

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#### Methods

- Washington University St. Louis PrEP Clinic, May-Aug 2016
- Urine & blood samples collected at routine clinic visits
- Eligibility: ≥18 years, on PrEP for ≥1 month, ≥1 urine TFV test
- Adherence definitions by method
  - Urine TFV levels >1000 ng/mL (dosing in the past 48 hours)
  - 3-Month MPR: 0.60 which is equivalent to 4 pills/week
  - Patient 7-day self-report (4 or 7 pills taken in last 7 days)
- Gold standard = urine TFV test
- Calculated sensitivity, specificity, PPV, and NPV of MPR and self report relative to urine TFV testing

#### Results



- 84 participants; 92 urine samples
- 84 participants
  - Median time on PrEP (IQR): 11 months (7-14)
  - Median age (IQR): 27 (24-33)
- 92 urine samples
  - 89% had urine TFV >1000 ng/mL
  - 94% (85/90) had 3-Month MPR ≥0.60
  - 89% had 7-day self-report ≥4 pills/week
  - 66% had 7-day self-report ≥7 pills/week

Participant Characteristics	N = 84	%
Age (Years)		
18-24	28	33.3
25-34	38	45.2
≥ 35	18	21.4
Gender		
Male	77	91.7
Female	6	7.1
Other	1	1.2
Race		
White	43	51.2
African American	28	33.3
Latino	5	6.0
Other/Mixed Race	8	9.5
Men who have sex with men	76	90.5
Education		
Less than college	28	33.3
College graduate	56	66.7



### Concordance of MPR and Self-report with urine TFV levels at 7 pills/week adherence

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		Urine TFV 10 -1000 ng/mL N (%)	>1000 ng/mL	Total N (%)
MPR <1.0	5 (83)	3 (75)	49 (61)	57 (63)
MPR ≥1.0	1 (17)	1 (25)	31 (38)	33 (37)
Total	6	4	80	90
Self-report <7 pills	5 (83)	3 (75)	23 (28)	31 (34)
Self-report 7 pills	1 (17)	1 (25)	59 (72)	61 (66)
Total	6	4	82	92

<sup>\*</sup>No significant difference found among age or race

# Concordance of MPR and Self-report with urine TFV levels at 4 pills/week adherence among MSM

		Urine TFV 10- 1000 ng/mL N (%)		Total N (%)
MPR < 0.60	2 (40)	2 (100)	1 (1)	5 (6)
MPR ≥0.60	3 (60)	0 (0)	74 (99)	77 (94)
Total	5	2	75	82
Self-report <4 pills	4 (80)	2 (100)	3 (4)	9 (11)
Self-report ≥4 pills	1 (20)	0 (0)	74 (96)	75 (89)
Total	5	2	77	84

	MPR	Pill/wk equivalent	Specificity (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	PPV (95% CI)
	1.00	7	80 (55-100)	14 (5-23)	39 (28-49)	94 (86-100)
	0.90	6-7	80 (55-100)	28 (11-44)	74 (64-83)	97 (92-100)
(	0.80	5-6	80 (55-100)	42 (20-64)	86 (79-94)	97 (93-100)
	0.70	4-5	50 (19-81)	50 (19-81)	94 (88-99)	94 (88-99)
	0.60	4-5	40 (10-70)	80 (45-100)	99 (96-100)	93 (93-87)
	0.50	3-4	40 (10-70)	100	100	93 (88-98)

<sup>\*</sup> Urine TFV adherence definition is > 1000 ng/mL

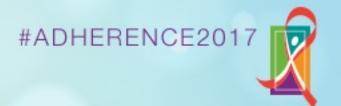
<sup>\*</sup> Specificity: Probability that MPR below cut off when urine TFV < 1000 ng/mL

<sup>\*</sup> Sensitivity: Probability that MPR above cutoff when urine TFV > 1000 ng/mL

<sup>\*</sup> Negative predictive value (NPV): Probability that the urine TFV < 1000 ng/mL when MPR is below cutoff

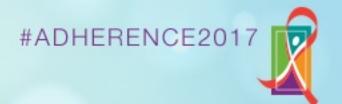
<sup>\*</sup> Positive predictive value (PPV): Probability that the urine TFV > 1000 ng/mL when MPR is above cutoff

<sup>\*\*</sup> A cutoff at 0.80 MPR or equivalent to on average 5-6 pills/week had the highest specificity and sensitivity for predicting adherence when compared to urine TFV (clinical relevance)



#### Limitations

- There were a low number of non-adherent patients in this study, which limits generalizability
- This patient population had few women
- Adherence methods measure different time periods (i.e. recent dosing for urine TFV vs. 3-Month MPR)
- The study includes repeat samples from the same patients
- MPR is a proxy of patient adherence



#### Conclusions

- There is a growing need to accurately and easily monitor PrEP adherence in clinical settings
- Urine TFV objectively screens for PrEP non-adherence
- MPR and self-report mapped out well onto urine TFV (used as a gold standard) with high sensitivity, specificity, PPV, and NPV
- Urine > 1000 ng/mL is highly concordant with MPR and self report suggestive of protective PrEP dosing (>4/wk)
- Urine < 10 ng/mL allows you to detect more nonadherence than MPR and self-report alone
- These measures can be used to enhance PrEP care

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