Metrics of Success: How to Measure Adherence to PrEP and Intermittent PrEP

Helen C. Koenig, MD, MPH
Medical Director, PrEP Program, Philadelphia FIGHT
Associate Professor, Infectious Diseases, University of Pennsylvania

Adherence 2018 • June 8-10 • Miami

Learning Objectives

- To discuss the role of objective adherence markers
- To discuss one short-term marker of adherence in greater detail
- To discuss the potential for point-of-care tests

Role of Objective Measures of Adherence

- Measures of self-report are subject to over-reporting bias and social-desirability bias
- Clinical trials have shown poor correlation of objective adherence markers with self-report in certain populations (youth, MSM of color, women)
- Drug-level feedback has been well-received in several studies
- There is currently no “perfect” objective adherence test
- There is imperfect correlation between different objective markers, likely due to biologic and analytic variability
- Only urine TFV testing is available currently outside the research setting, although not yet reimbursable by insurance

Van Damme et al, NEJM 2012; Marrazzo JM et al, NEJM 2015; Baxi SM et al, JAIDS 2015; Agot K et al, AIDS Behav 2014; Koester KA et al, AIDS Care 2015; Koenig HC et al, HIV Med 2017; Landovitz RJ, JAIDS 2017; Baxi SM et al, PLOSOne 2018

Urine TFV Assay

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

- Methods: Liquid chromatography/mass spectrometry assay
- Advantages:
  - Non-invasive, acceptable to target population
  - Affordable, easily incorporated into a variety of settings
  - Low maintenance adherence monitoring strategy
  - Can be collected at the same time as urine STI screening, etc.
  - Stable for up to 14 days at room temperature and with standard refrigeration

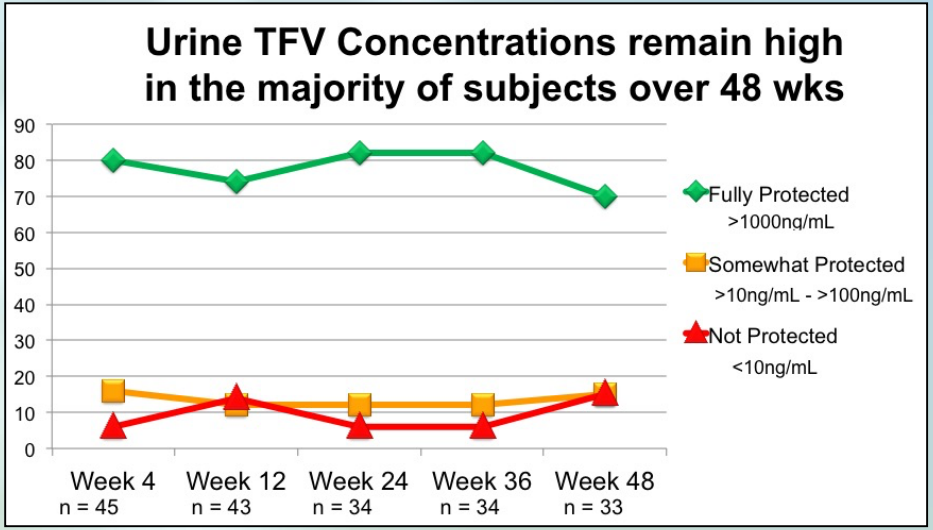
Koenig CROI 2015

Urine TFV test: Performance Characteristics

Analytical Validation	How well does the test perform in the laboratory?	Urine testing vs Plasma (n = 10)	Sensitivity	100%
			Specificity	100%
			PPV	100%
			NPV	100%
		CDC Validation of Urine Test (n = 50)	Sensitivity	94%
			Specificity	91%
			PPV	85%
			NPV	97%
Clinical Validation	How well does the test perform in a clinical setting?	Urine testing (dose in last 48 hrs) vs DBS (>4 doses/wk) (n = 90)	Sensitivity	94%
			Specificity	56%
			PPV	95%
			NPV	50%
Clinical Utility	How useful is the test?	Adherence study in real world setting (n = 50)	Week 4	80%
			Week 12	74%
			Week 24	82%
			Week 36	82%
			Week 48	70%
		Validated in patients on TAF-based regimens (n = 10)	“Urine testing detects TFV in HIV patients on TAF-based treatment” (Oral Abstract Presentation Session 1)	

Retention and Adherence Remain High Through 48 wks

Retention (n=50)	%	% Adjusted for "Out-of-Window" PrEP pick-ups
Week 12	84	90
Week 24	62	74
Week 36	62	70
Week 48	50	70



Lalley-Chareczko L et al, CROI 2017

Potential for point-of-care testing

- A point-of-care (POC) objective adherence tool could be very helpful in identifying patients with low- or non-adherence
  - Could be an early marker of someone who may become lost-to-care
  - Could have great impact in the developing world where real-time results are critical, as it can be challenging to bring people back in for results
- POC testing options are currently being developed for several measures, including DBS, whole blood, and urine
- Research priorities:
  - Understanding how these measures could be combined to most accurately assess adherence patterns and drug exposure
  - Finding a test (or tests) that are affordable, logistically feasible, and clinically relevant
  - Determining the best way to give adherence results in a positive rather than punitive way