

HIV Pre-Exposure Prophylaxis (PrEP) Medication Monitoring

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Disclosures

Only FTC/TDF (Truvada), FTC/TAF (Descovy), and CAB-LA (Apretude) are currently approved by the U.S. Food and Drug Administration (FDA) and only for use in some but not all populations.

This talk may include discussion of non-FDA approved strategies for HIV prevention.

Disclaimer

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Terminology (updated May 2, 2024)

“Adherence” was previously recommended over “compliance” to reflect active engagement in care.

Stigmatizing Terms To Avoid	Use These Alternatives	Here’s Why
Treatment default	<ul style="list-style-type: none"> ✓ Treatment non-completion ✓ Interruption in treatment 	<p>“Default” is a negative term that implies judgment about the person who did not complete treatment.</p>
Compliance <i>Related terms to avoid: adherence/adherent*</i>	<ul style="list-style-type: none"> ✓ Continuity of treatment ✓ Continuity of care ✓ Taken as prescribed 	<p>“Compliance” implies passive behavior/ following instructions or orders. *While “adherence/adherent” is preferred to “compliance,” using “continuity of treatment” or “continuity of care” acknowledges that sometimes treatment is interrupted due to circumstances beyond a person’s control.</p> <p>This language shift is intended to focus on the circumstances (whether treatment is occurring for any reason) vs. the presumption that access to and taking of medicine is entirely at the will of the individual. Continuation of medication is not limited to treatment and should be revisited when discussing taking medications for PrEP use as well. “Taken as prescribed” provides a clear alternative that suggests that medication is taken whether needed daily or monthly.</p>

Topics To Be Covered

- Review
 - Relationship with efficacy
 - Challenges of oral PrEP medication monitoring
- Novel strategies for oral PrEP medication monitoring
 - Ingestible sensors
 - Urine monitoring

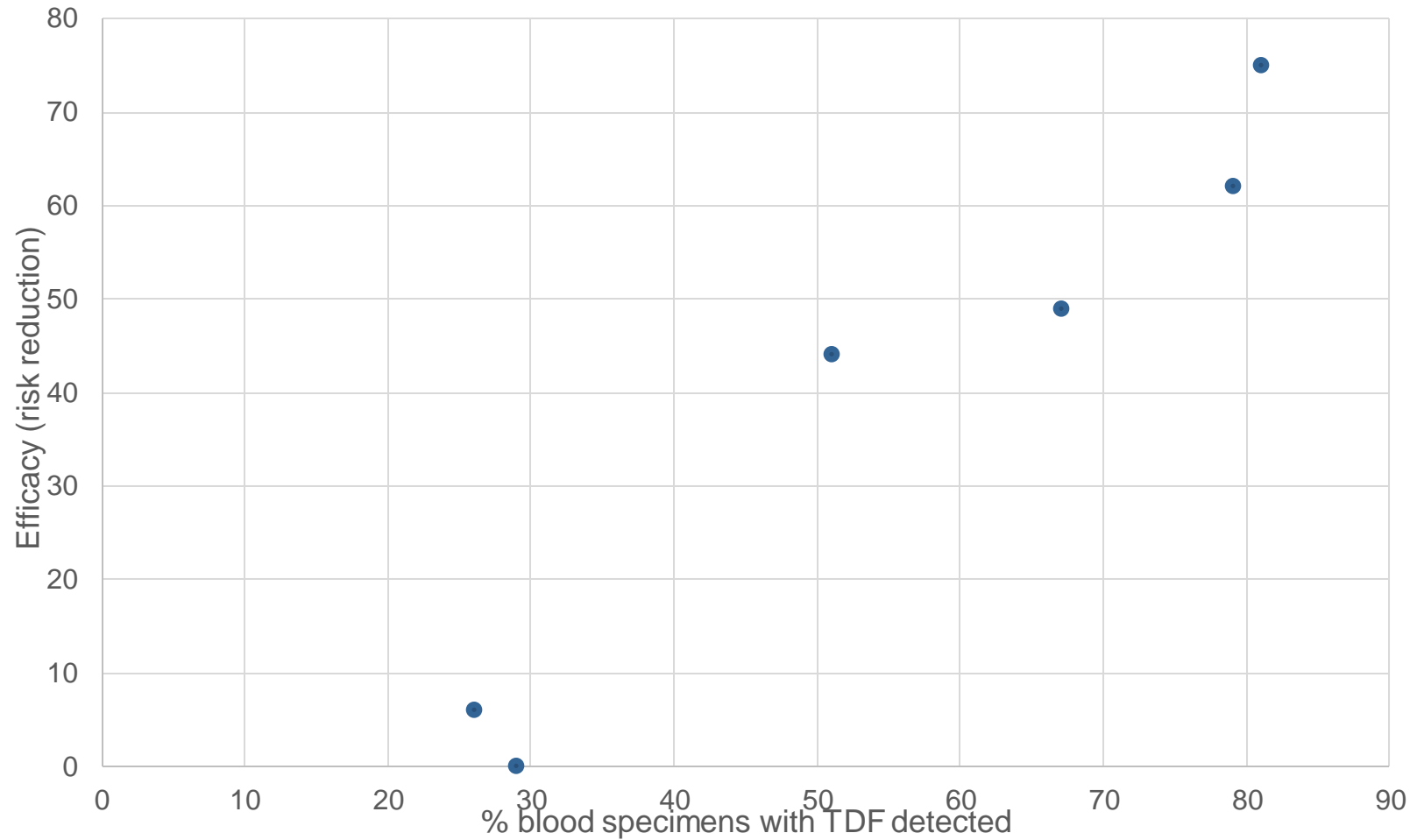
The Relationship Between PrEP-Taking and Efficacy

	Efficacy in randomized comparison	% of blood samples with tenofovir detected
Partners PrEP	75%	81%
TDF2	62%	79%
Bangkok TDF	49%	67%
iPrEx	44%	51%
FEM-PrEP	6%	26%
VOICE	-	29%

Baeten et al N Engl J Med 2012
Grant et al N Engl J Med 2010
Choopanya et al Lancet 2013

Van Damme et al N Engl J Med 2012
Thigpen et al N Engl J Med 2012
Marrazzo et al N Engl J Med 2015

The Relationship Between PrEP-Taking and Efficacy

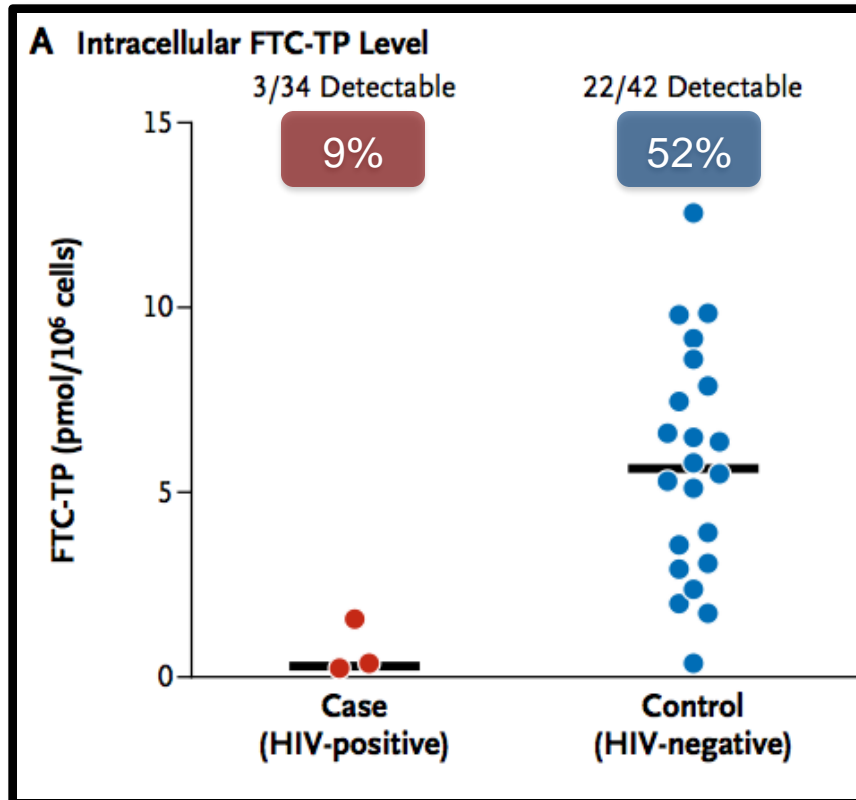


Baeten et al N Engl J Med 2012
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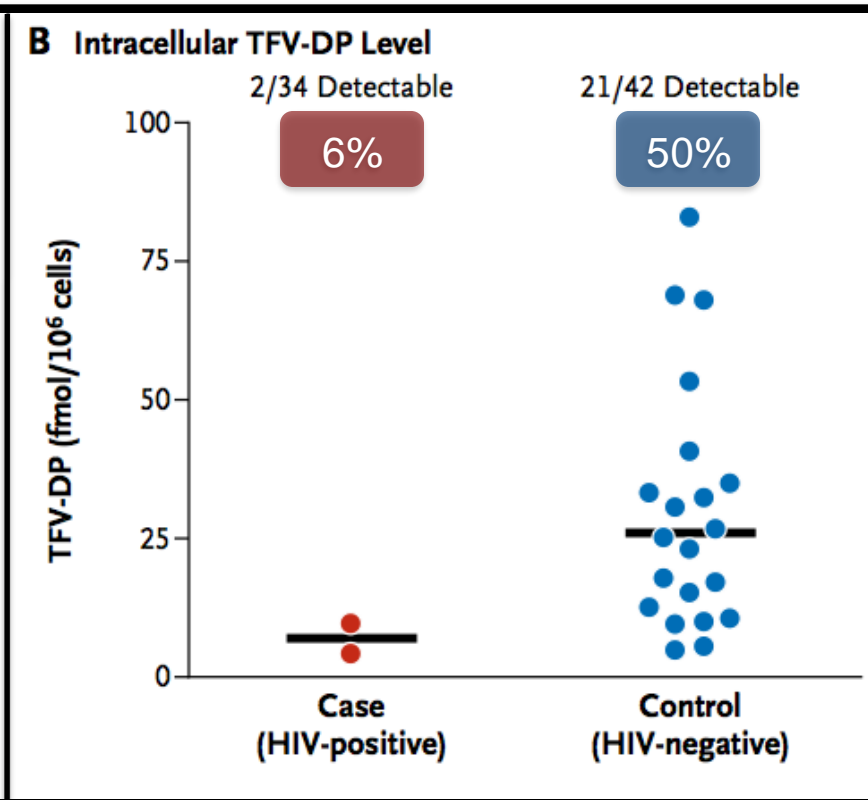
Van Damme et al N Engl J Med 2012
Thigpen et al N Engl J Med 2012
Marrazzo et al N Engl J Med 2015

The Relationship Between PrEP-Taking and Efficacy Lessons from iPrEx

A. Intracellular Emtricitabine Levels



B. Intracellular Tenofovir-DF Levels



Adjusted RR reduction (any detectable level) = 95%

Source: Grant RM, et al. N Engl J Med. 2010;363:2587-99.

PrEP Medication Monitoring

Available Tools

For PWH

- Viral load = surrogate biological marker

For PrEP

- Self-report
- Pharmacy refills
- Pill counts
- Electronic monitoring (pillboxes, smartwatches, apps)
- Ingestible sensors
- Drug level testing

How to Monitor PrEP

Self-report and simple measures

- 1) Does your patient show up to appointments?
- 2) Did your patient pick up their prescriptions?
- 3) Single questions: “Many people find it difficult to take a medicine every day. Thinking about the last week, how many days have you not taken your medicine?”

alternatives:

How many days have you not taken your medicine in the last month?

How good has your pill-taking been over the last month?

(very poor, poor, fair, good, very good, excellent)

How to Monitor PrEP

Available Tools: Electronic Systems



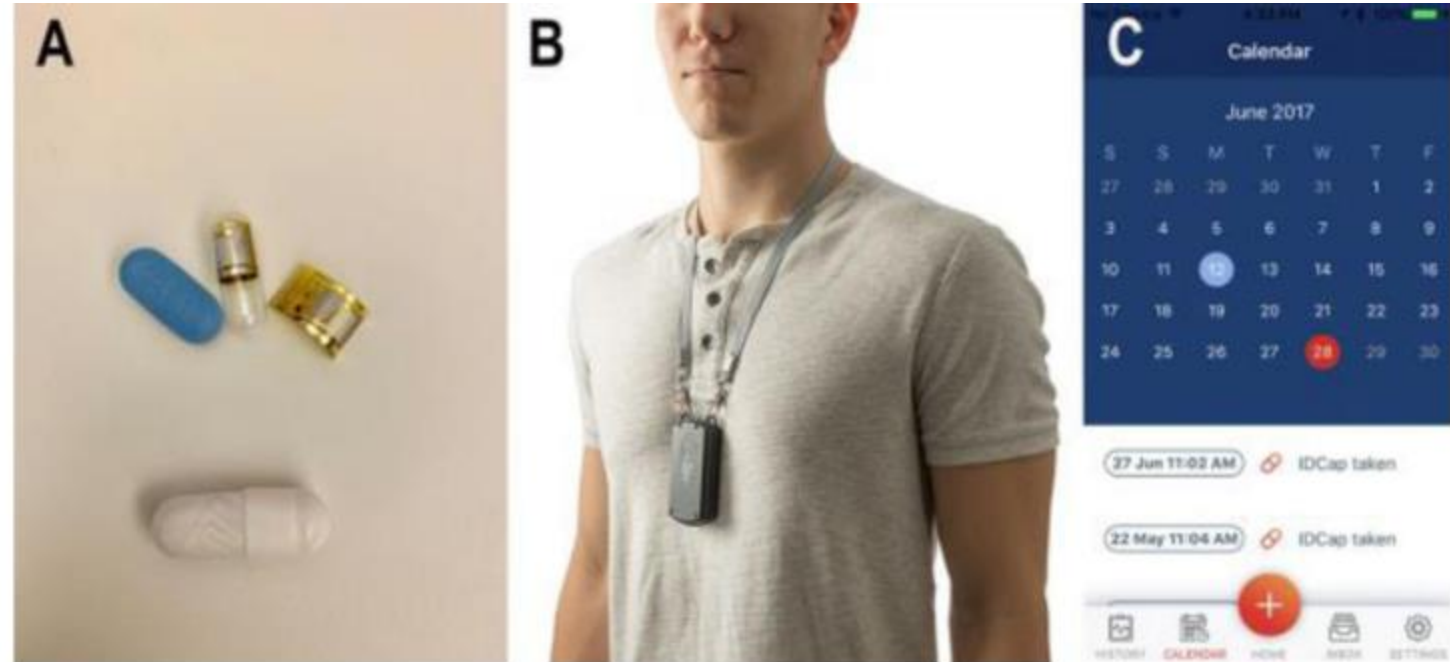
Wisepill: Koss et al. CID 2018; 66(2): 213-219

Medisafe: Morawski et al; JAMA Internal Med 2018; 178(6): 802-809

How to Monitor PrEP

Available Tools: Ingestible Sensors (Digital Pill Systems)

- Radiofrequency sensor in gelatin capsule
- Sensor activated by chloride ions in gastric fluid
- Radiofrequency signal read by the wearable reader
- Ingestion data relayed by Bluetooth to app
- One digital pill was FDA approved in 2017



How to Monitor PrEP

Available Tools: Drug Level Testing

- Blood plasma
 - exposure window 2-7 days
- TFV-DP in PBMC
 - exposure window 7-14 days
- TFV-DP in DBS
 - exposure window 1-2 months
 - must be standardized against hemoglobin
- Hair
 - 50-100 strands collected close to scalp
 - exposure window weeks to months, 1 cm hair = 1 month

All strongly correlated

All use liquid chromatography/mass spectrometry

Results cannot be provided in real time

How to Monitor PrEP

Available Tools: Point-of-care drug level testing

- Urine tenofovir (TFV) concentration strongly correlated to plasma
- Short-term marker
- Antibody-based immunoassays (ELISA) can detect TFV
- Lateral flow assays reduce complexity/cost
- Urine TFV monitoring is acceptable to patients

How to Monitor PrEP

Available Tools: Point-of-care drug level testing in urine

Goals

- identify dosing with 24 hours
- maximize “specificity”

(minimize people inappropriately identified as not taking their pills as prescribed)

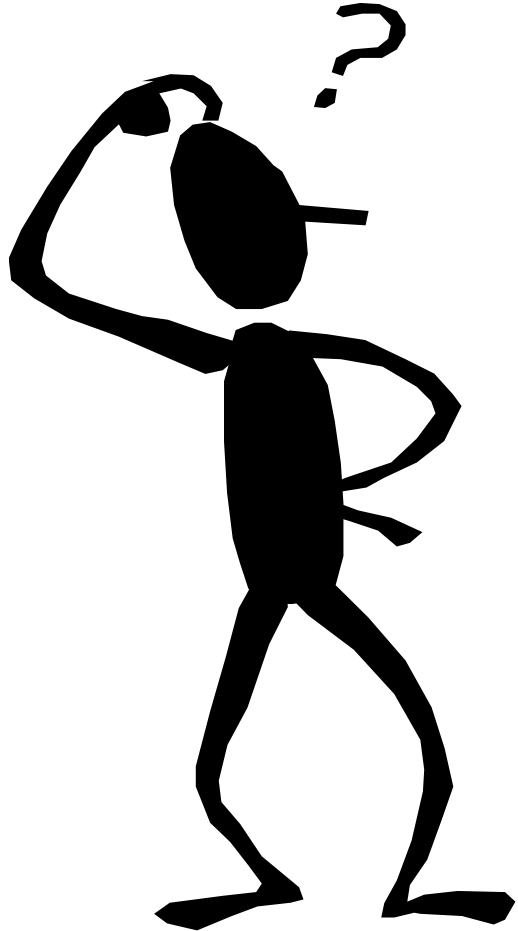
Hours since last dose	Probability <1000ng/mL	Probability <1500ng/mL	Probability <2000ng/mL
12	0%	1%	1%
24	1%	2%	5%
48	8%	16%	25%
72	35%	52%	63%
96	74%	86%	91%
120	95%	98%	99%

1500ng/mL selected as threshold for this POC test

Use of point-of-care drug level testing in urine

- Low urine TFV predicted seroconversion in iPrEx OLE, Partners PrEP
 - Spinelli AIDS 2019;33(5):867-872; Stalter CID 2021;72(3):486-489
- Real-time counseling based on urine POC results increased detectable urine levels in PrEP patients in Kenya
 - Spinelli 2023 Adherence (Conference), abstract #1302, Gandhi 2024 CROI.
- Ongoing studies:
 - Post-partum women in S. Africa, MSM in CA, adults in Thailand
 - Validation of FTC/TAF
 - Measurements of long-term adherence
- UrSure (Daughtridge & Koenig) purchased by OraSure in 2020
 - SureSight TFV-DP test (through Molecular Testing Labs)
 - SureQuick urine POC test (research use only)

Questions?



Acknowledgment

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