Pharmacologic Measures of PrEP Adherence among High-Risk MSM in HPTN 067

Jennifer Velloza[1], Monica Gandhi[2], Craig W. Hendrix[3], Peter Bacchetti[2], Pamela Murnane[2], James Hughes[1], Maoji Li[4], Marcel Curlin[5,6,7], Timothy H. Holtz[5,6], Sharon Mannheimer[8], Mark A. Marzinke[3], K. Rivet Amico[9], Estelle Piwowar-Manning[3], Susan H. Eshleman[3], Robert M. Grant[2,10]

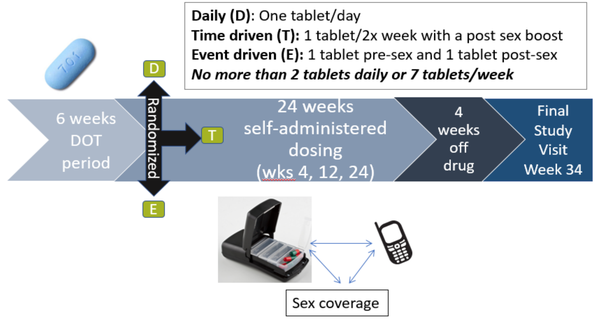
[1]University of Washington, Seattle, USA; [2]University of California at San Francisco, San Francisco, USA; [3]Johns Hopkins University, Baltimore, USA; [4]Fred Hutchinson Cancer Research Center, Seattle, USA; [5]US Centers for Disease Control & Prevention, Atlanta, USA; [6]Thailand MOPH- US CDC Collaboration, Bangkok, Thailand; [7]Oregon Health & Science University, Portland, USA; [8]Columbia University, New York, USA; [9]University of Michigan, Ann Arbor, USA; [10]Gladstone Institute of Virology & Immunology, San Francisco, USA

BACKGROUND

- The effectiveness of oral emtricitabine (FTC)/tenofovir (TFV) disoproxil-fumarate pre-exposure prophylaxis (PrEP) depends on adherence.
- Self-reported adherence measures are limited by recall and social desirability bias.
- Pill counts and electronic monitoring devices (e.g., Wisepill™, MEMS caps) can record the number of pills removed but not actual drug consumption.
- Pharmacologic measures are useful for understanding patterns of adherence and identifying predictors of PrEP use. Comparing these measures to one another and electronic data can guide adherence interpretation in PrEP settings.

METHODS

- HPTN 067/ADAPT was a randomized trial of intermittent and daily PrEP (PMID: 28986029, 29143163)
- Data collection and follow-up concluded in 2014
- Participants randomly assigned to daily, time-, or event-driven oral PrEP regimens
- Study visits at weeks 0, 4, 12, and 24 post randomization
- Plasma and hair samples at each visit to assess FTC and TFV concentrations; Wisepill™ and sexual behavior data collected weekly
- This analysis included 350 men who have sex with men (MSM) enrolled in Bangkok, Thailand and Harlem, United States.
  - -Estimated Pearson correlation coefficients among measures
  - -Linear mixed models to assess predictors of log-transformed plasma (short-term) and hair (longer-term) concentrations of TFV/FTC



RESULTS

Table 1. Participant characteristics at enrollment (N=350)[1]

Arm	
Daily arm	116 (33.1%)
Event-driven arm	117 (33.4%)
Time-driven arm	117 (33.4%)
Site	
Bangkok, Thailand	176 (50.3%)
Harlem, USA	174 (49.7%)
Age, years	31 (25-38)
Secondary school or less education	171 (48.9%)
AUDIT score ≥8[2]	73 (20.9%)
Number of sex partners in prior 3 months	4 (2-8)
Any HIV-positive sex partners in prior 3 months	44 (12.6%)
Any unprotected sex in prior 3 months	264 (75.4%)

[1]N (%) or Median (IQR); [2]Indicative of heavy alcohol use

Figure 1. Correlations between PrEP pill-taking measures

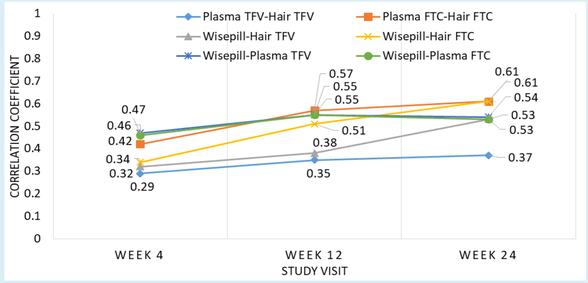


Table 2. Pill-taking and sexual behavior during follow-up[1]

	Daily	Event-Driven	Time-Driven
PrEP doses/week, from Wisepill data	6.0 (3.7-6.7)	1.4 (0.7-2.4)	2.2 (1.8-2.8)
Number of sex acts during follow-up	7 (4-13)	7 (3-13)	6 (2-13)

[1]Data presented are Median (IQR)

Table 3. Estimated multivariate associations of covariates with hair and plasma drug concentrations[1]

	Hair Drug Concentrations		Plasma Drug Concentrations	
	TFV (n=381 visits)	FTC (n=379 visits)	TFV (n=946 visits)	FTC (n=946 visits)
Covariate	Adjusted Effect (95% CI)		Adjusted Effect (95% CI)	
Time-driven	**-0.45 (-0.82, -0.09)**	**-0.69 (-1.13, -0.26)**	**-0.39 (-0.96, 0.18)**	**-0.50 (-1.20, 0.19)**
Event-driven	**-0.97 (-1.37, -0.57)**	**-1.57 (-2.03, -1.11)**	**-2.26 (-2.85, -1.68)**	**-2.71 (-3.40, -2.01)**
Daily	**----**	**----**	**----**	**----**
Harlem	**-0.70 (-1.16, -0.23)**	**-1.13 (-1.55, -0.71)**	**-0.65 (-1.22, -0.09)**	-0.53 (-1.22, 0.16)
Bangkok	**----**	**----**	**----**	Reference
Age, years	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.02)	**0.03 (0.01, 0.06)**	**0.04 (0.01, 0.07)**
≤ Secondary	-0.37 (-0.85, 0.11)	**-0.57 (-0.99, -0.15)**	-0.54 (-1.10, 0.03)	-0.64 (-1.33, 0.05)
College	----	**----**	**----**	**----**
AUDIT ≥8	**0.40 (0.03, 0.77)**	**0.50 (0.15, 0.86)**	0.20 (-0.24, 0.63)	0.33 (-0.22, 0.89)
# sex acts since prior visit[2]	0.21 (-0.02, 0.45)	0.14 (-0.11, 0.39)	**0.28 (0.02, 0.54)**	**0.38 (0.07, 0.69)**
Time*Sex Acts	**-0.14 (-0.40, 0.11)**	**-0.05 (-0.34, 0.24)**	-0.14 (-0.49, 0.21)	-0.24 (-0.66, 0.19)
Event*Sex Acts	**0.17 (-1.17, 0.44)**	**0.36 (0.07, 0.66)**	0.26 (-0.14, 0.65)	0.21 (-0.26, 0.68)
Daily*Sex Acts	**----**	**----**	----	----

[1]Models included all covariates shown here. TFV and FTC concentrations are log-transformed. Significant effects (p-value <0.05) are highlighted; [2]Measured per 10 sex acts

CONCLUSIONS

- Among MSM in HPTN 067, plasma and hair drug concentrations and Wisepill™ data were correlated with one another.
- Site, study arm, education, age, alcohol use, and sexual risk were differentially associated with long-and-short term pill-taking behavior (e.g., age was associated with short-term but not long-term pill-taking)
- Patterns of pill-taking can be assessed by examining plasma and hair concentrations of PrEP drugs in conjunction

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For more information, please contact: Jennifer Velloza, jvelloza@uw.edu

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