



# Pharmacologic drug detection and self-reported adherence in the HPTN069/ACTG5305 Phase II PrEP trial

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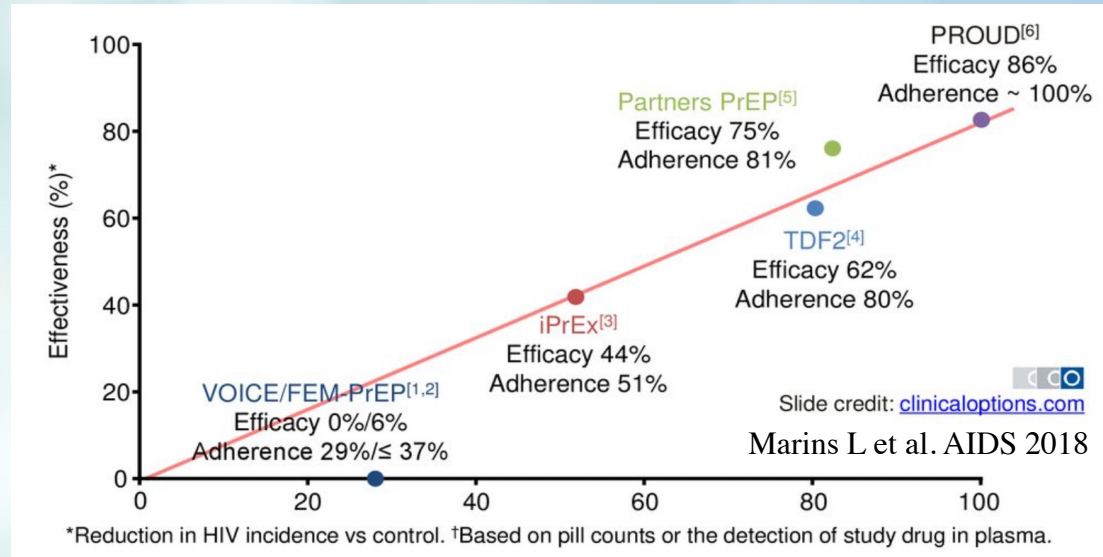
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# Background

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- **Adherence** drives efficacy in oral PrEP clinical trials
- Several past clinical trials have demonstrated inaccuracies of self-reported PrEP adherence<sup>1-5</sup>
- More recent studies, which have become increasingly pragmatic, have found that the discrepancy between pharmacologic and self-reported indicators of adherence are narrowing<sup>6-8</sup>



Drug levels associated with PrEP efficacy



# Aims

- To assess objective **pharmacologic-based adherence** and subjective **self-reported adherence** among individuals participating in a PrEP candidate clinical trial
- Characterize demographic predictors of patient estimation of reported PrEP adherence

# Design

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- Deidentified data from **HPTN 069/ACTG A5305<sup>9-10</sup>**
  - Randomized, double-blind Phase II study of the safety/tolerability of 3 candidate PrEP regimens and 1 demonstrated control regimen (each arm consisting of 3 tablets) at 13 sites in the United States and Puerto Rico
    1. **Maraviroc (MVC) + 2 Placebo**
    2. **MVC + Emtricitabine (FTC) + Placebo**
    3. **MCV + Tenofovir (TDF) + Placebo**
    4. **TDF + FTC + Placebo [Control]**

## Weeks 24 and 48

**Drug concentrations:** TDF, FTC, and MVC by plasma samples

**Self-reported adherence:** Computer-assisted self interview (CASI surveys)

Descriptive statistics and a generalized linear model with repeat visits for statistical evaluation

9. Gulick RM, et al. *J Infect Dis.* 2017.

10. Gulick RM, et al. *Ann Intern Med.* 2017.

# Correlates of Interest

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## Correlates:

- Sex assigned at birth
- Age
- Race/ethnicity
- Education level
- Employment Status
- Marital Status
- Report of active illicit drug use
- Psychological scales





# Drug Concentration Testing

## Tenofovir and Emtricitabine

- **Plasma drug concentrations** at study week 24 and 48
- Classified as daily or less-than-daily adherence by using established benchmarks from HPTN 066 Directly Observed Therapy (DOT) study (threshold optimized for  $\geq 90\%$  sensitivity)<sup>11</sup>

### Daily Adherence:

- TFV: concentration  $\geq 35.5$  ng/ml
- FTC: concentration  $\geq 49.1$  ng/ml

# Drug Concentration Testing

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## Maraviroc

No established MVC benchmark from a DOT study

- MVC threshold estimated by conducting ROC analysis from HPTN 069 MVC + TDF and MVC + FTC arms to ensure concentrations that were consistent with daily drug use

Estimated a **MVC threshold of 4.1 ng/ml** for 100% sensitivity

Follow-up analysis:

Percent of samples classified as daily drug use was examined across the four study arms and two time periods

- 4.1 ng/ml benchmark in MVC only arm yielded a value that closely corresponded to the other three arms from HPTN 066 (TDF/FTC Directly Observed Therapy) benchmarks

# Self-Reported Adherence

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## 3 CASI Items (Week 24 and Week 48)

1. Ability to take study medication every day in the past month  
**(Excellent, Very Good, Good, Fair, Poor, Very Poor)**
2. How much of the study drug was taken as recommended in the past month  
**(0 – 100%, slider)**
3. Over the past month, how much of the time was study drug taken as recommended  
**(All of the time, most of the time, half of the time, some of the time, none of the time)**





# Self-Reported Adherence

- Item responses linearly transformed to a 0 – 100 point scale  
(Summary of the individual adherence items calculated as the mean of the three individual items)
- Daily adherence for composite scores equal to or greater than **96**  
(Reflecting reports of perfect or near perfect adherence on a linearized Wilson 3-item measure summary<sup>12</sup>)

# Baseline Demographics

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Sex at birth	
Male	440 (61%)
Female	278 (39%)
Age at Enrollment	
Median	32
Race	
Black	308 (43%)
White	353 (49%)
Ethnicity	
Hispanic/Latino	131 (18%)

## Education Level

High School or Less 207 (29%)

College or Higher 268 (37%)

## Employment Status

Unemployed 265 (37%)

Employed 453 (63%)

## Marital Status

Single/Widowed 466 (65%)

Partnered/Married 246 (34%)

## Psychological Scales

Anxiety/Depression 179 (25%)

## Illicit Drug Use

Active Drug Use 410 (57%)

# Results

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## **370 participants**

(Enrollment Phase I: 227 cisgender men/2 transgender women; Enrollment Phase II: 140 cisgender women/1 transgender man)

Table 1: Frequency of adherence by self-report and drug-concentrations

	Daily adherence		Total
	Self-reported daily adherence in past month	Self-reported less than daily adherence in past month	
Drug level reflects daily adherence	225	242	467(65%)
Drug level reflects non-daily adherence	81	170	251(35%)
Total	306(43%)	412(57%)	718(100%)

**65%** had drug concentrations consistent with daily adherence  
**43%** had CASI survey responses reporting daily adherence



# Odds of Adherent Drug Concentration

<u>Covariates</u>	<u>Univariate analyses:</u>	<u>Multivariate analyses:</u>
<b>Male Assigned at Birth</b>	OR <b>2.19</b> [95% CI 1.91, 2.52]	aOR <b>1.42</b> [95% CI 1.02, 1.97]
<b>Older</b> (per 5 year increase)	OR <b>1.05</b> [95% CI 1.03, 1.06]	aOR <b>1.10</b> [95% CI 1.09, 1.11]
<b>White</b>	OR <b>3.33</b> [95% CI 2.85, 3.84]	aOR <b>2.20</b> [95% CI 1.88, 2.56]
<b>Advanced Education</b>	OR <b>8.08</b> [95% CI 6.28, 10.39]	aOR <b>3.89</b> [95% CI 2.97, 5.09]
<b>Employed</b>	OR <b>3.39</b> [95% CI 3.10, 3.71]	aOR <b>1.89</b> [95% CI 1.50, 2.40]
<b>Married/Partnered</b>	OR <b>1.75</b> [95% 1.72, 2.12]	aOR <b>2.00</b> [95% 1.72, 2.32]

# Self-Reported Adherence

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## with Non-Adherent Drug Concentrations

Among participants with drug concentrations suggesting non-daily dosing (N=251), the following groups were **more likely to self-report daily adherence** (N=81) than less than daily adherence (N=170)

<u>Covariates</u>	<u>Univariate analyses:</u>	<u>Multivariate analyses:</u>
<b>Male</b>		
<b>Assigned at Birth</b>	aOR <b>1.26</b> [95% CI 1.05, 1.51]	aOR <b>1.24</b> [95% CI 1.20, 1.29]
<b>Older</b> (per 5 year increase)	aOR <b>1.10</b> [95% CI 1.08, 1.11]	aOR <b>1.09</b> [95% CI 1.09, 1.09]
<b>White</b>	aOR <b>1.20</b> [95% CI 1.05, 1.38]	aOR <b>1.28</b> [95% CI 1.05, 1.56]



# Conclusions

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- **65%** of participants in HPTN 069 had drug concentrations consistent with daily medication adherence
  - Among these, **48%** reported daily/near daily adherence over the past month on self-report measures
- However, less than half (**43%**) self-reported daily adherence
- **Male, older, White, college-educated, employed, and/or partnered/married** participants were more likely to have drug concentrations reflecting daily adherence
- However, **male, older, and white** participants were also more likely to overestimate their medication adherence by self-report when drug concentrations suggested less than daily adherence

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(SCHARP)**

**Study Participants**

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