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BACKGROUND

- ADAPT: **A**lternative **D**osing to **A**ugment **P**rEP pill **T**aking
- Phase 2, randomized, open-label study of non-daily oral emtricitabine/tenofovir disoproxil fumarate pre-exposure prophylaxis (PrEP)
- Silom Community Clinic CRS, Bangkok, Thailand, was one of three study sites
- Primary results presented at IAS 2015, Vancouver BC
- Oral PrEP is efficacious for prevention of sexual HIV acquisition¹
- “On Demand” PrEP was also found to be efficacious in the IPERGAY study in France and Canada²
- PrEP dosing before and after sex is effective for MSM taking on average 16 doses per month³
- Adherence is the critical determinant of effectiveness⁴
- Adapting PrEP regimens to match infrequent or episodic sexual exposure could increase adherence and minimize medication costs and side effects
- Understanding predictors of PrEP coverage of sex acts could assist in increasing adherence and coverage of PrEP

¹Grant NEJM 2010; Baeten NEJM 2012; Thigpen NEJM 2012; Choopanya Lancet 2013; ²Molina NEJM 2015; ³Grant Lancet ID 2014; ⁴Anderson, Donnell, Van Damme, Marrazzo

OBJECTIVE

- Primary outcomes in the HPTN 067 study were coverage of sex events, number of tablets required and taken, and self-reported side effects
- In this analysis we sought to identify baseline predictors of PrEP coverage of sex events among participants at the Bangkok CRS

ELIGIBILITY

- MSM and TGW were eligible if:**
 - Male at birth
 - Reported anal intercourse with another male in the past 6 months
 - Reported ≥ 1 other HIV risk factor in the past 6 months
 - Normal renal function (CrCl > 70 ml/min)
- Exclusion criteria included:**
 - HIV infection
 - Hepatitis B infection
 - Symptoms of acute HIV
 - Use of nephrotoxic drugs
 - Proteinuria or glucosuria or low serum phosphate
 - Recent PEP or PrEP use

METHODS

METHODS FOR STUDY

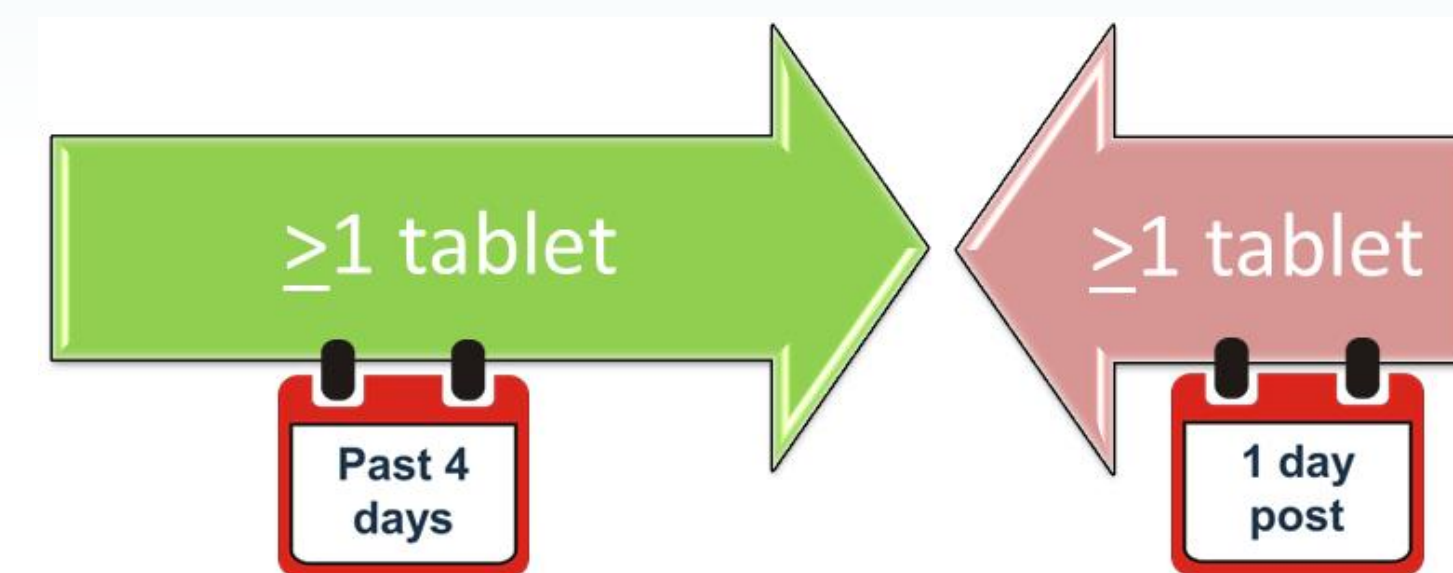
- Study began with a 6 week DOT lead-in phase
- Participants were randomized 1:1:1 to 24 weeks of one of three self-administered PrEP dosing strategies:
 - Daily: 1 tablet daily
 - Time-driven: 1 tablet twice a week plus 1 tab post-sex
 - Event-driven: 1 tablet 24-48 hours before and 1 tab within 2 hours after sex
- Bangkok was one of three study sites
- We contacted participants weekly to collect dates/times of PrEP use (monitored electronically by the Wisepill™ dispensing device) and sex events
- Participants filled out a computer-assisted self interview (CASI) about sexual behavior and frequency at screening, 6, 18, and 30 weeks
- Participants who acquired HIV infection at any point during the study discontinued dosing and were followed until study closure and referred for post-trial care

METHODS FOR CURRENT ANALYSIS

- Data from Bangkok CRS only
- Alcohol (AUDIT score) and substance use were assessed by computer-assisted self-interview
- Used sex act as the unit of analysis
- We used general estimating equations for clustered data to evaluate predictors associated with coverage
- Coverage and adherence assessed without use of plasma concentrations

DEFINITION: COVERED EVENT

Coverage for all arms:
 ≥ 1 pill taken in the 4 days before sex
 ≥ 1 pill taken in the 24 hours after sex



LIMITATIONS

- All coverage and adherence measures are limited by subjective measurement
- Sexual event was based on self report
- Coverage defined by the protocol is insufficient to approximate efficacy

RESULTS

PARTICIPANT CHARACTERISTICS: BANGKOK

TABLE 1. Participant Characteristics, Bangkok

Variable	% (N=178)
Median age (years, IQR)	31 (27,34)
Age ranges	
18-20	1%
21-25	21%
26-30	28%
31-35	30%
36-40	14%
>40	6%
Gender identity	
Male	99%
TGW	1%
Race	
Asian	100%
Never married	97%
Education	
Completed college	83%
In college, not completed	6%
Unemployed	11%
Student	9%

RESULTS PRESENTED AT IAS 2015

- Among Thai MSM, coverage (85%) and adherence (85%) and drug concentrations were highest in the daily arm
- Compared with the daily regimen (85%), the time-driven dosing regimens offered comparably high PrEP coverage (84%) for sex acts with fewer tablets required
- In all arms, when a dose required for full coverage was missed, it was usually the post-sex dose
- Adherence was greater in the daily arm (85%) compared with the time-driven arm (at 79%) or event-driven arm (at 65%), no statistically significant difference between daily and time-driven arms in adherence
- Compared with the daily arm, the number of doses required for full adherence was reduced by 56% in the time-driven arm and by 80% in the event-driven arm ($p < 0.001$)
- 2 seroconversions during the 6-week pre-randomization weekly DOT study phase, both occurred at week 4; No seroconversions during the self-administered phase
- Study results offer additional support for current CDC guidelines for daily PrEP dosing

SUBSTANCE USE BASELINE RESULTS

- Use of substances at baseline:
 - stimulants (e.g. amphetamine type) (8.4%)
 - marijuana (2.8%)
 - opiates (1.7%)
 - other drugs (23%)
- AUDIT scores indicated moderate alcohol use in 20.8% and high alcohol use in 6.7%

PREDICTOR ANALYSIS

- Proportion of covered sex acts by those reporting stimulant use (coverage: 74%) was similar to those reporting other drug use (non-alcohol) (76%, $p = 0.80$), but lower than those reporting no substance use (85%, $p = 0.04$)
- In a multivariable model those factors associated with higher coverage included:
 - Age 25–35 years (adjusted odds ratio [aOR] 2.34, 95% CI 1.37–3.97, $p = 0.002$); age < 25 years as referent
 - Completion of college (aOR 1.74, 95% CI 1.04–2.92, $p = 0.03$)
 - Moderate (AUDIT Score 7–12: aOR 1.75, 95% CI 1.15–2.66, $p < 0.01$) to high levels (AUDIT Score >13: aOR 2.86, 95% CI 1.19–6.86, $p = 0.02$) of alcohol use
- In a multivariable model those factors associated with lower coverage included:
 - Higher number of reported sex events (13–80 over three months at baseline: aOR 0.57, 95% CI 0.32–1.00, $p = 0.05$); 0-4 reported sex events as referent
 - Use of stimulant drugs (aOR 0.47, 95% CI 0.24–0.93, $p = 0.03$)

TABLE 2. Univariate and Multivariate Analysis of Factors Associated with Higher Coverage of Sex Events, Bangkok HPTN 067/ADAPT Study (N=178)

Characteristic	OR	p value	Adjusted OR*	95% CI	p value
Age (years)					
<25			Ref	--	
25-35	1.68	0.03	2.34	1.37–3.97	0.002
>35	1.13	0.78	1.68	0.95–2.97	0.07
Education					
College completion	1.65	0.21	1.74	1.04–2.92	0.03
Sex events/3 months					
0-4			Ref	--	
5-12	0.66	0.11	0.65	0.35–1.21	0.18
13-80	0.55	0.04	0.57	0.32–1.00	0.05
AUDIT score†					
0-6			Ref	--	
7-12	1.49	0.07	1.75	1.15–2.66	<0.01
≥ 13	1.31	0.47	2.86	1.19–6.86	0.02
Reported drug use type					
No drug use			Ref	--	
Stimulants with or without others	0.52	0.04	0.47	0.24–0.93	0.03
Other illicit drugs only	0.59	0.15	0.76	0.49–1.15	0.20

* Characteristics considered in the model included study arm, age, employment, education, alcohol use (AUDIT), drug use type, depression score, and in the past 3 months the reported number of sex events, number of sex partners reported, and reported condomless sex.
 † The Alcohol Use Disorders Identification Test (AUDIT) is a simple ten-question test developed by WHO to determine if a person may be at risk for alcohol abuse problems.

CONCLUSION

- Higher coverage of sex acts with PrEP was associated with a college education, and moderate to high (AUDIT score) baseline alcohol use, after adjusting for age
- Baseline use of stimulants and higher sexual frequency in the past 3 months was associated with lower coverage
- Regardless of substance use, the majority of Thai MSM/TGW followed the regimen dosing schedules to provide coverage of sexual exposures with PrEP

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