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How Do You Like Your PrEP?

Results from the HPTN 067/ADAPT Study

Presented by Robert Grant, MD, MPH
on behalf of the HPTN 067/ADAPT Study Team

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Background

- Oral FTC/TDF PrEP is effective for preventing HIV acquisition.[1]
  - Full protection after rectal exposure with use of 4+ tabs/week.[2]
  - Full protection after vaginal exposure likely requires more PrEP use.[3]
- Sex is often planned, and plans change over time.[4]
  - PrEP provides benefit when used during seasons of risk.[5]
  - Such strategic PrEP use has been observed in MSM.[2]
  - Measurement of adherence is challenging, especially when dynamic.[6]
- Recommending PrEP dosing before and after sex was effective among MSM.[7]
- ***Study Premise**: Adapting PrEP regimens to match patterns of sex could increase strategic PrEP use and minimize medication costs and side effects.*

1. Grant *NEJM* 2010, Baeten *NEJM* 2012, Thigpen *NEJM* 2012, Choopanya *Lancet* 2013;
2. Grant *Lancet Infec. Dis.* 2014, Liu *JAMA Int. Med.* 2015; 3. Grant *AIDS* 2015, Cottrell *JID* 2016;
4. van Griensven *JIAS* 2010, 5. Hojilla *AIDS and Behavior* 2015, Grant *Lancet* 2016
6. Mutua *PLoS One* 2012, Kibengo *PLoS One* 2013; 7. Molina *NEJM* 2015.

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HPTN 067 Design

FTC/TDF

Daily- One tablet/day
Time driven- 1 tablet/2x week with a post sex boost
Event driven- 1 tablet pre-sex and 1 tablet post-sex
No more than 2 tablets daily or 7 tablets/week

Women (incl. TGW) & MSM

6 weeks DOT period

Randomized

D

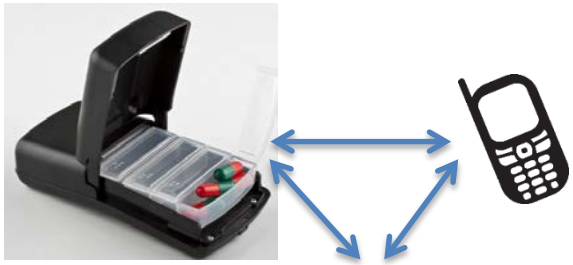
T

E

24 weeks self-administered dosing

4 weeks off drug

Final Study Visit Week 34



PrEP use and sex

Key informant interviews and focus groups

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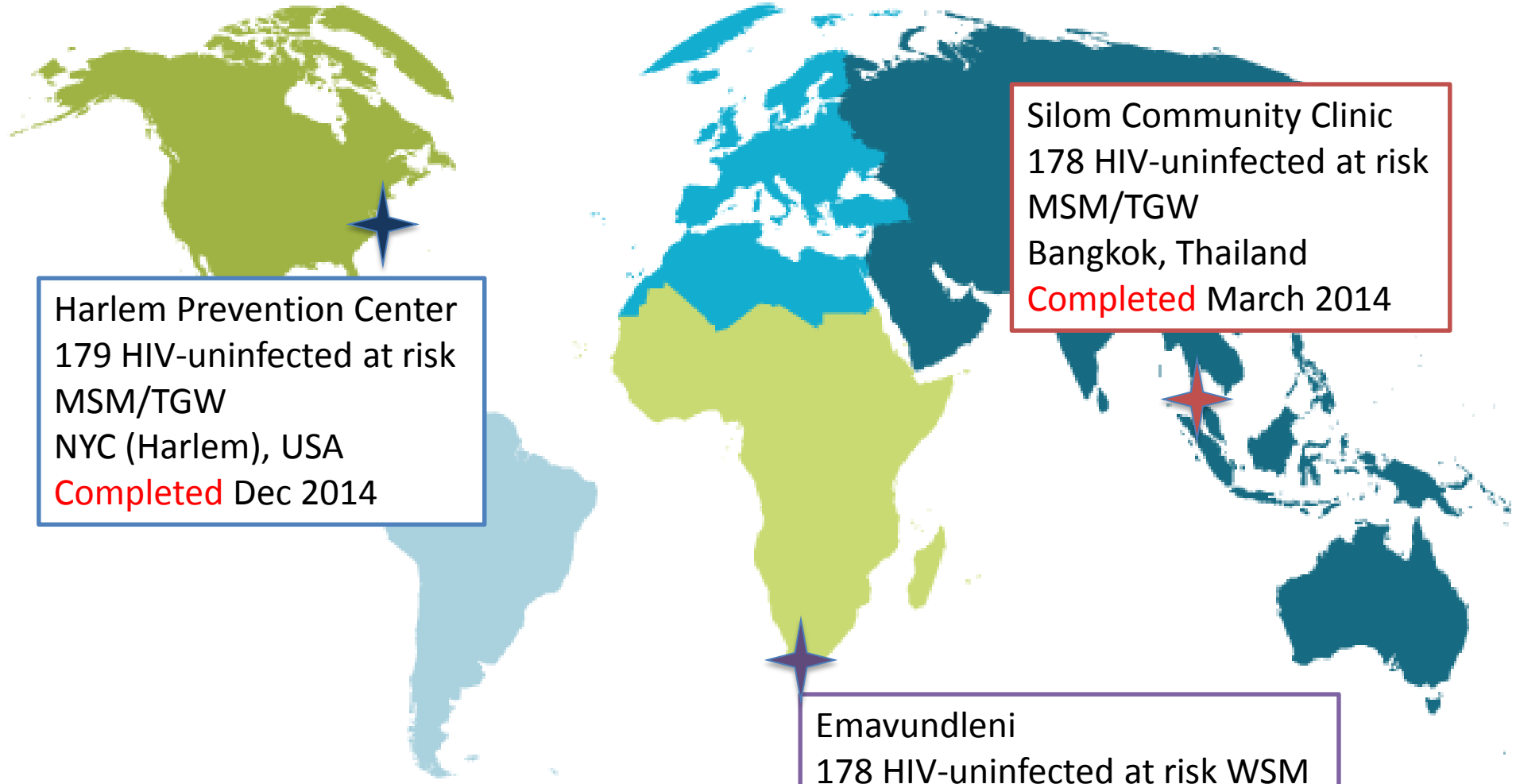

Harlem Prevention Center
179 HIV-uninfected at risk MSM/TGW
NYC (Harlem), USA
Completed Dec 2014

Silom Community Clinic
178 HIV-uninfected at risk MSM/TGW
Bangkok, Thailand
Completed March 2014

Emavundleni
178 HIV-uninfected at risk WSM
Cape Town, South Africa
Completed June 2013

Definition: Coverage

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

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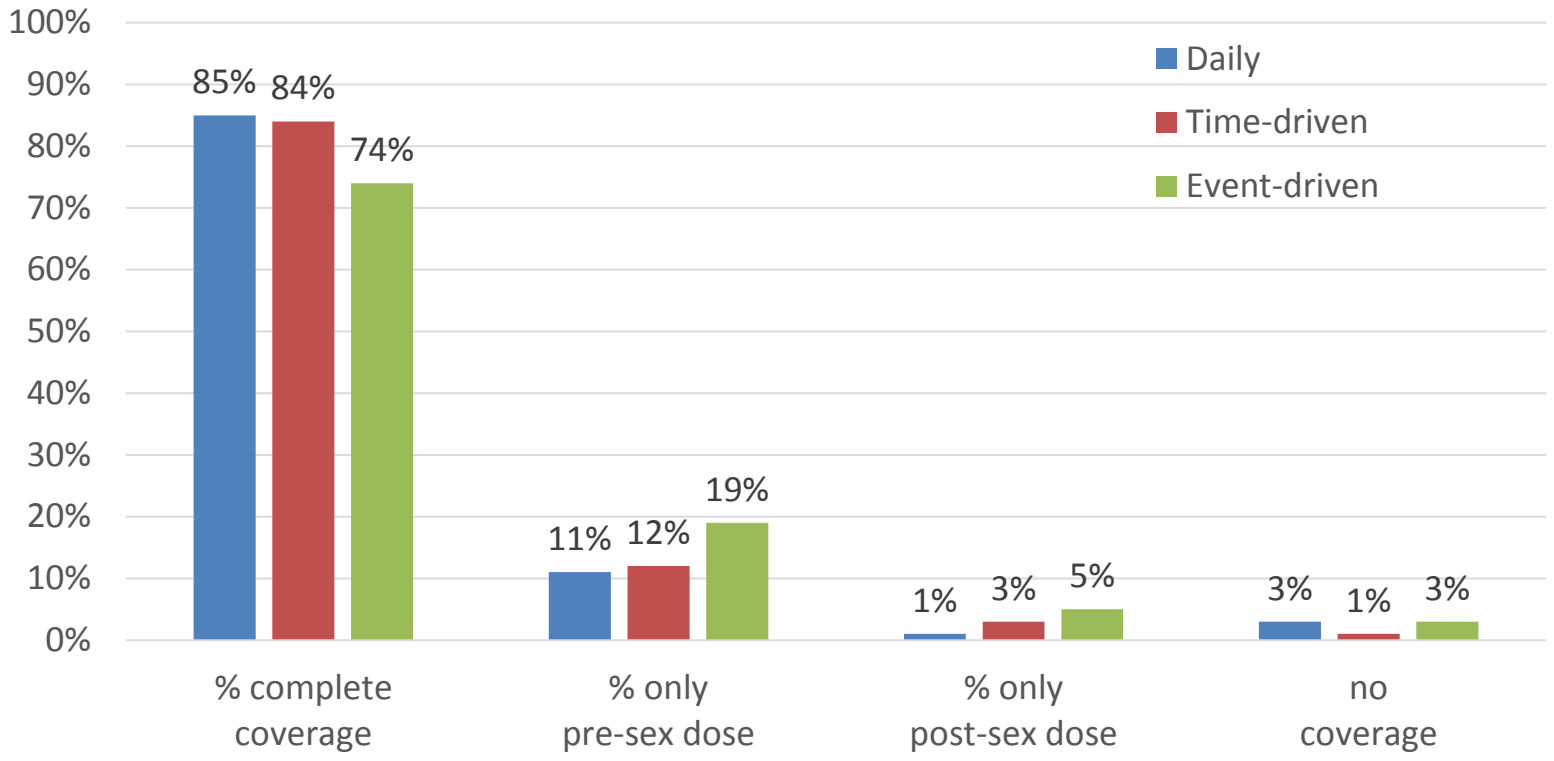
Coverage of Sex Events – MSM/TGW in Bangkok



Daily/Time $p = 0.79$, Daily/Event $p = 0.02$, Time/Event $p = 0.04$, global $p = 0.19$

Holtz, IAS 2015, Vancouver

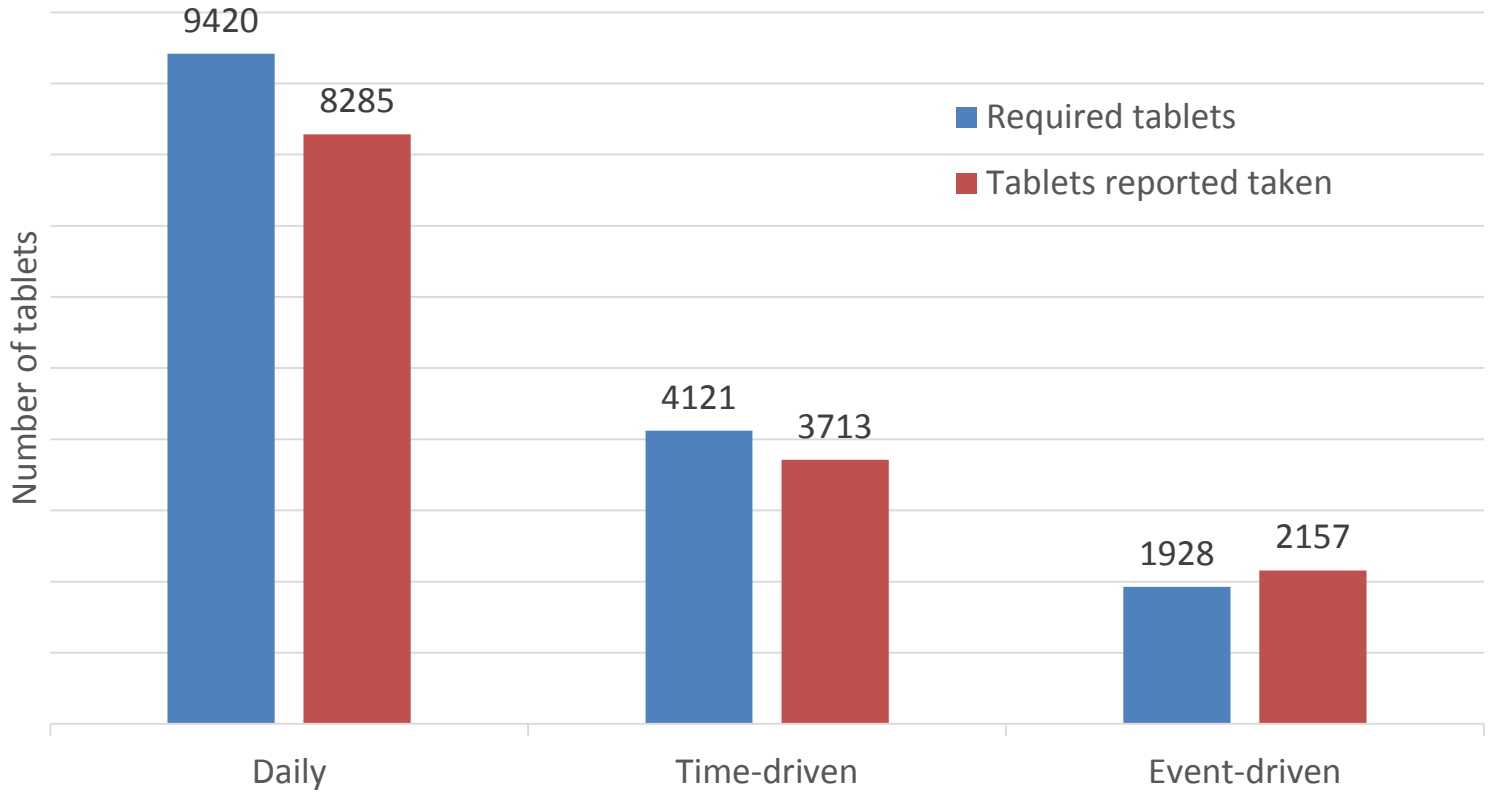
Tenofovir diphosphate in PBMCs: % with TFVDP >= 5.2 fmol/10^6 cells* Bangkok MSM/TGW

Participants who report sex in last 7 days with detectable TFVDP in PBMC (>=5.2 fmol/10^6 cells)	Daily (D)	Time-driven (T)	Event-driven (E)
Week 10	31/31 (100%)	29/29 (100%)	30/30 (100%)
Week 18	28/29 (96.6%)	30/30 (100%)	24/26 (92.3%)
Week 30	22/23 (95.7%)	18/19 (94.7%)	13/14 (92.9%)

*Indicative of at least 2 tablets per week.

Time/Daily p = 0.60, Event/Daily p = 0.51, Time/Event p=0.28

FTC/TDF Pills by Arm
MSM/TGW in BKK HPTN 067/ADAPT

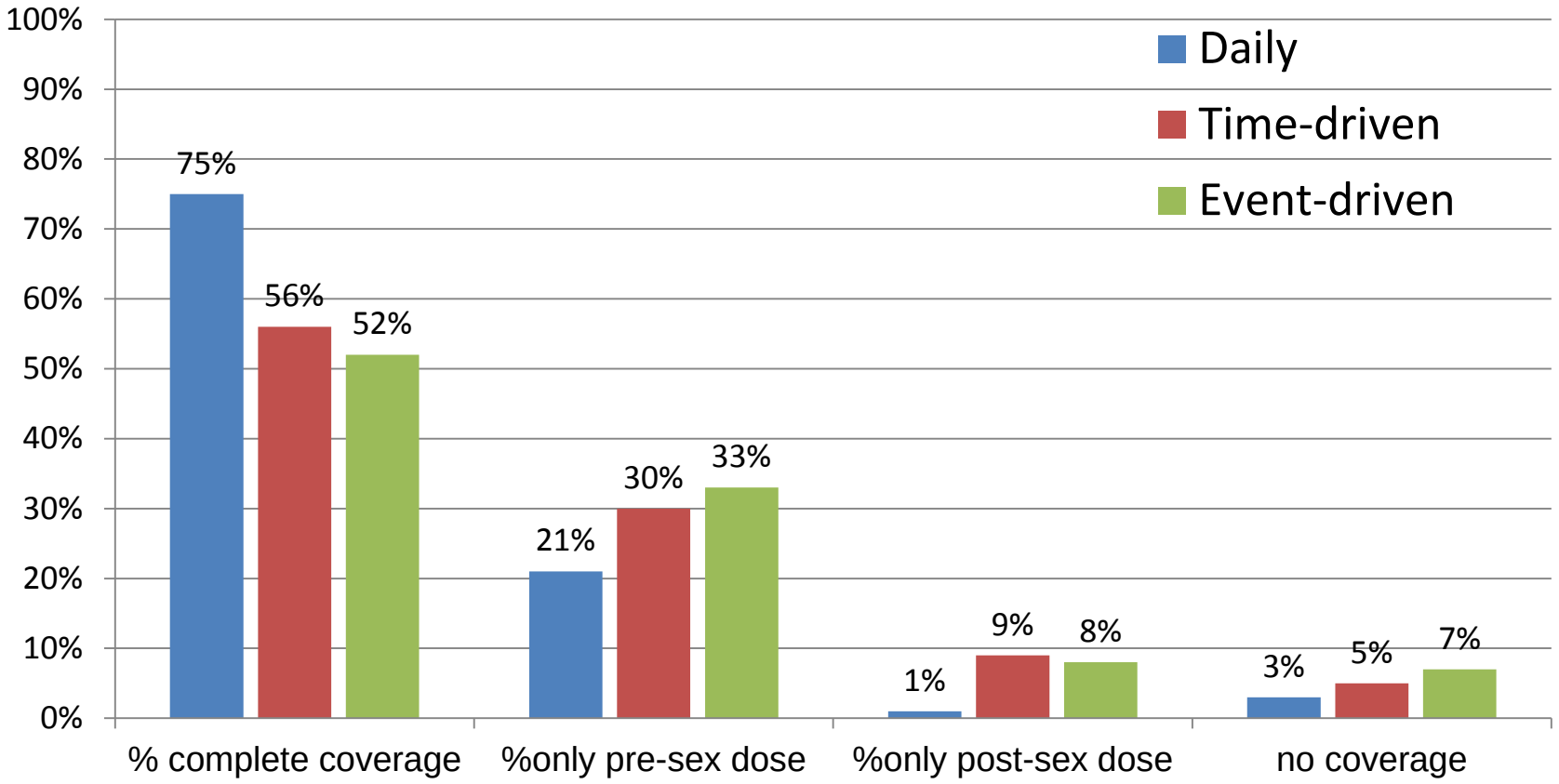


Required tablets: $p < 0.001$ for all comparisons (D/T, D/E, and T/E)
Tablets actually taken: $p < 0.001$ for all comparisons (D/T, D/E, and T/E)

Neuro and GI Symptoms / Side Effects MSM/TGW in Bangkok HPTN 067/ADAPT

Side Effect reported on Structured Interview	Daily	Time	Event	*p* value
% PPTs who experienced any neurologic side effects	48%	46%	54%	0.64
% PPTs who experienced any GI side effects	45%	34%	41%	0.46

Coverage of Sex Events – Women in Cape Town



Sex event defined as vaginal or anal intercourse
Time/Daily p = 0.0007, Event/Daily p < 0.0001, Time/Event p = 0.43

Bekker IAS2015, Vancouver, 2015

TFVDF in PBMCs:

% with TFVDP >= 5.2 fmol/10^6 cells

PBMC* - Cape Town

Participants who report sex in last 7 days with detectable TFV-DP in PBMC (>=5.2 fmol/10^6 cells)	Daily (D)	Time-driven (T)	Event-driven (E)
Week 10	33/40 (82.5%)	16/23 (69.6%)	25/37 (67.6%)
Week 18	29/39 (74.4%)	16/25 (64.0%)	10/30 (33.3%)
Week 30	19/29 (65.5%)	13/24 (54.2%)	12/31 (38.7%)

*Indicative of at least 2 tablets per week.

Time/Daily p = 0.16, Event/Daily p = 0.002, Time/Event p=0.13

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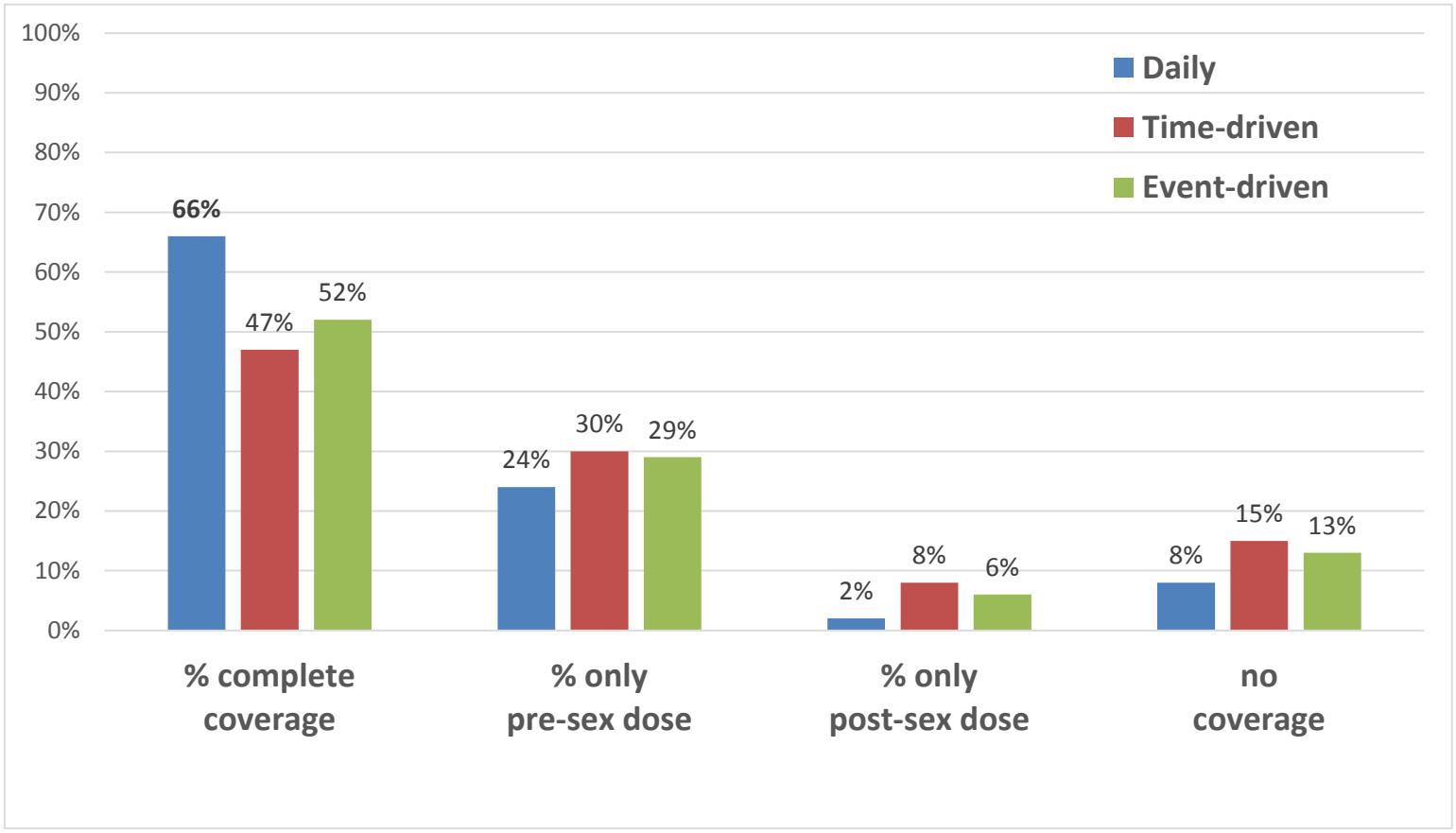
Coverage of Sex Events – MSM/TGW in NYC



Time/Daily and Event/Daily p = 0.01; Time/Event p =0.47

Mannheimer, IAS 2015, Vancouver

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TFVDF in DBS:
% with TFVDP >= 326 FMOLE/punch
DBS* - Harlem

Participants who report sex in last 7 days with detectable TFV-DP in DBS (>=326 fmole/punch)	Daily (D)	Time-driven (T)	Event-driven (E)
Week 10	13/23 (56.5%)	8/23 (34.8%)	5/27 (18.5%)
Week 18	11/27 (40.7%)	10/27 (37.0%)	3/21 (14.3%)
Week 30	9/18 (50.0%)	3/18 (16.7%)	3/18 (16.7%)

*Indicative of at least 2 tablets per week.

Time/Daily p = 0.11, Event/Daily p = 0.004, Time/Event p=0.13

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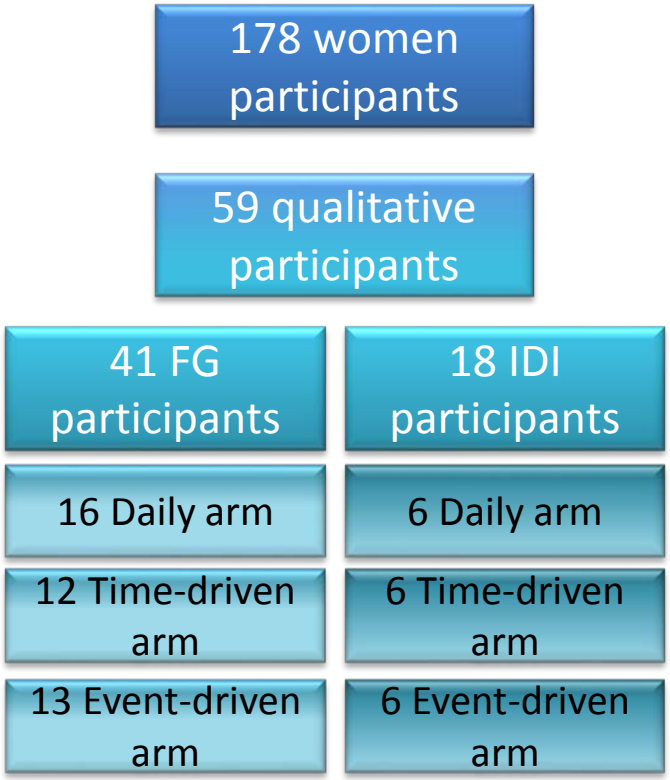
Qualitative Methods Cape Town



- Average age 26, range 18-44
- On self-administered PrEP for 24 weeks
- Qualitative data collected within 3-months of final study visit

Amico, Mutuality Model, *AIDS and* Behavior, in press

Distrust	Uncertainty	Alignment	Mutuality
Different Questions About PrEP			
Whatever…	*What?*	*How?*	*Now!*
Different Goals for the Care Team			
Build Trust For Disclosure	*Support Exploration With Information*	*Identify Barriers & Facilitators & Build Skills*	*Let Her Lead*

Adapted from Amico, **Mutuality Model**, *AIDS and Behavior, in press*

Conclusions

- Adherence to oral PrEP is feasible in diverse groups.
- A recommendation for daily PrEP dosing led to…
  - Highest coverage,
  - Highest adherence,
  - Highest PrEP drug concentrations,
  - Higher pill burden.
- Time-driven dosing led to…
  - Comparable PrEP coverage in Bangkok MSM.
- Health care strategies should be adapted to the level of engagement on the mutuality spectrum.

Limitations and Next Steps

- Participants were informed that daily dosing was proven to be effective, and that non-daily dosing was unproven.
  - This information likely undermined motivation to use non-daily regimens.
- Insights to guide when to start and stop PrEP are emerging from clinical practice.
- Active surveillance of PrEP seroconversions would provide more information about dosing strategies and outcomes.

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