





UNIVERSITY OF WASHINGTON INTERNATIONAL CLINICAL RESEARCH CENTER

# Prevention-Effective Adherence in a Demonstration Project of PrEP among HIV Serodiscordant Couples in East Africa

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### Declarations

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#### Adherence and efficacy in PrEP trials



% adherence

**HIV protection effectiveness** 

(with permission from J. Baeten)

# Adherence has been high in demonstration projects to date

	Partners Demonstration Project	The Demo Project	Project ADEPT
Deputation	Serodiscordant couples	MSM	Young women
Population	(East Africa)	(US)	(South Africa)
Adherence	85% by TFV	80-86% of TFV consistent with 4+ doses/week	79%
HIV incidence (per 100 person years)	0.2	0.4	

(Baeten et al, CROI 2015; Liu et al, JAMA IM 2016; Bekker et al, CROI 2015)

#### Prevention-effective adherence

(a) Paradigm for ART and clinical trials: Success is achieved through 100% adherence.



(b) <u>Prevention-effective adherence paradigm</u>: Success is achieved because PrEP is used during all episodes of HIV exposure. Adherence to PrEP may be periodic and mapped to periods of risk.



(Haberer et al, AIDS 2015)

### Prevention-effective adherence



Understanding prevention-effective adherence requires knowledge of dynamic risk behaviors and concurrent use of multiple prevention strategies

#### Partners Demonstration Project

- Open-label study of integrated PrEP and ART among 1,013 high-risk (>5% estimated incidence) serodiscordant couples in 4 sites in East Africa
- HIV-uninfected partner encouraged to take PrEP until HIV-infected partner had taken ART for 6 months ("bridge strategy")
- 24 months follow-up with quarterly visits

## Methods

- Analysis reflects 12 months of follow-up per participant
- Adherence measured with MEMS
  Based on PrEP as dispensed
  - Per participant preference
  - Per protocol (i.e., study holds)
  - Data censored if adherence >120% (N=9)
  - Average doses/week in month prior to a study visit



#### Definitions of risk



#### Definitions of risk





# Definitions of sufficient adherence

- 4+ doses/week for MSM (Anderson et al, Sci Tran Med, 2012)
- 6+ doses/week for women (Cottrell et al, JID, 2016)
- Unclear what is needed for heterosexual men

# Analysis

- Prevention-effective adherence defined descriptively
- Predictors of prevention-effective adherence assessed by multivariable repeated measures regression
  - Socio-demographics
  - Reported risk
  - Concerns/beliefs about PrEP Abuse
  - Relationship characteristics
    Pregnancy intention
  - Sexual activity
- A priori gender interactions
- Variables assessed for collinearity

- Problem alcohol use
- Depression

#### Participant characteristics (at enrollment)

	N (%) or median (IQR)
Male	656 (67%)
Age (years)	29 (26-36)
Education (years)	8 (6-12)
Number of children with study partner	0 (0-2)
Unprotected sex with study partner in past month	638 (67%)
Unprotected sex with non-study partner in past month	60 (6%)
CD4 count of HIV-infected partner	437 (271-640)
HIV RNA of HIV-infected partner (log <sub>10</sub> )	4.6 (3.9-5.0)

#### High overall PrEP initiation and adherence

- PrEP initiation: 985 of 1,013 (97%) participants
  - 960 at enrollment
  - 20 at Month 1
  - 5 at Month 3+
- Overall MEMS adherence
  - Median = 88% (IQR 65-98%)
  - Mean = 78% (SD 27%)

# Study months with prevention-effective adherence

Total N= 3,156 study months

		Risk of HIV acquisition						
		High		Рі	Probable		Low	
Sufficient adherence (doses/week)	Total visits	N visits	% high risk visits	N visits	% probable risk visits	N visits	% low risk visits	p-value
4+	2,556	475	87%	1,807	83%	274	62%	<0.0001
6+	2,120	392	72%	1,514	70%	214	49%	<0.0001

- People know how to adhere when they are at risk
- Achieving sufficient adherence is easier with a lower threshold

#### Predictors of prevention-effective adherence (sufficient adherence = 4+ doses/week)

Predictor	RR	95% CI	p-value
No concerns about daily PrEP	1.24	1.12 - 1.39	<0.0001
Pregnancy intentions			0.034
Not pregnant, not trying	ref		
Not pregnant, trying	1.05	1.00 - 1.11	
Current partnership pregnancy	1.05	1.00 - 1.10	
Partner on ART >6 months	0.94	0.88 - 1.00	0.038
No longer in couple w/ study partner	0.76	0.64 - 0.91	0.001

- Non-significant: age 25+ years\*, study month enrollment, any condom use, any sex, sex with or without condoms, social support, want relationship to succeed
- 155 study-months (<5%) excluded due to missing data

\*p=0.055

#### Predictors of prevention-effective adherence (sufficient adherence = 6+ doses/week)

Predictor	RR	95% CI	p-value
Sex risk with study partner in past 30 days			0.008
No sex with study partner	ref		
Had sex w/ study partner, all protected	1.44	1.07 - 1.95	
Had sex w/ study partner, any unprotected	1.52	1.12 - 2.05	
No concerns about daily PrEP	1.34	1.16 - 1.55	<0.0001
Want desperately/very much for relationship to succeed	1.17	1.04 - 1.33	0.007
Age 25+ (years)	1.13	1.03 - 1.24	0.008
Female	1.08	1.01 - 1.16	0.023
Has problem alcohol use	0.88	0.81 - 0.96	0.003
In follow up >6 study months	0.87	0.81 - 0.93	<0.0001
No longer in couple w/ study partner	0.63	0.49 - 0.81	<0.0001

- Not significant: study month enrollment, married to study partner, any condom use, any sex, any sex, abuse in partnership, CD4 count
- No significant gender interaction terms in either model

## Conclusions

- PrEP adherence is different than ART adherence
- Most people are achieving prevention-effective adherence
- Adherence is higher in those at higher risk
- Achieving prevention-effective adherence is more challenging when the threshold for protection is higher

## Implications

- Predictors may help identify PrEP candidates
  - No concerns about taking a daily pill
  - Aware of risk (e.g., being sexually active in a serodiscordant couple)
  - Commitment to something that may be achieved through PrEP (e.g., relationship)
- Predictors may be helpful in targeting support
  - Enabling factors above
  - E.g., problem alcohol use, age <25 years</p>

#### **Partners Demonstration Project Team**

#### Investigators

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#### **Research participants**



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## Thank you!

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