



MASSACHUSETTS
GENERAL HOSPITAL

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HARVARD
MEDICAL SCHOOL

Pros and Cons of On Demand PrEP

« Cons »

Jessica Haberer, MD, MS

June 6, 2017

IAPAC Adherence Conference



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Pros and Cons of On Demand PrEP « Issues »

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Disclosures

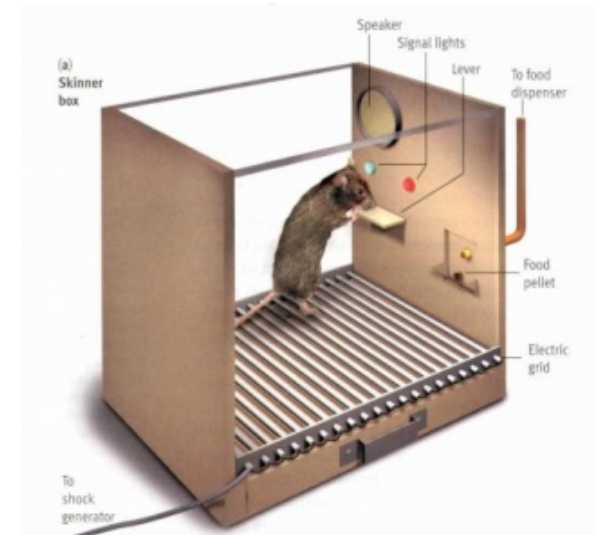
- I have no conflicts to declare
- I receive grant funding through the NIH, Gates Foundation and USAID
- I have been a consultant for the NIH, WHO, and Merck
- I own stock in Natera

Outline

- Habit formation
- How much PrEP is enough PrEP?
- Prevention-effective adherence
- Parting thoughts

Habit formation

- Habit: “A more or less fixed way of thinking, willing, or feeling acquired through previous repetition of a mental experience”
(*Am J Psychol*, 1903)
- Habit formation
 - Cue
 - Daily PrEP = Typically non-sexual behavior
(e.g., brushing teeth, news program, alarm)
 - On demand PrEP = Sex
 - Behavior = Taking PrEP
 - Reward = HIV protection, reduced stress in relationships, etc



Which cue works?

- It depends
- IPERGAY suggests sex works as cue for MSM choosing to take on demand PrEP
- IAVI pilot RCT of intermittent* PrEP showed it did not work well (MEMS)
*Intermittent = Monday, Friday + post-coital (max 1 dose/day)

	Daily PrEP	Intermittent PrEP	Post-coital
Kenya (MSM)	83%	55%	26%
Uganda (couples)	98%	91%	45%

- Difference may have been related to knowledge of efficacy and choice
- Measurement may also play a role

(Mutua, PLoS One, 2012; Kibengo, PLoS One, 2013)

Individual preference

Table 3

Stated likelihood of using different preexposure prophylaxis modalities for HIV infection among 1106 men who have sex with men, aged 18–34 years, participating in an online survey, United States, April–July 2015.

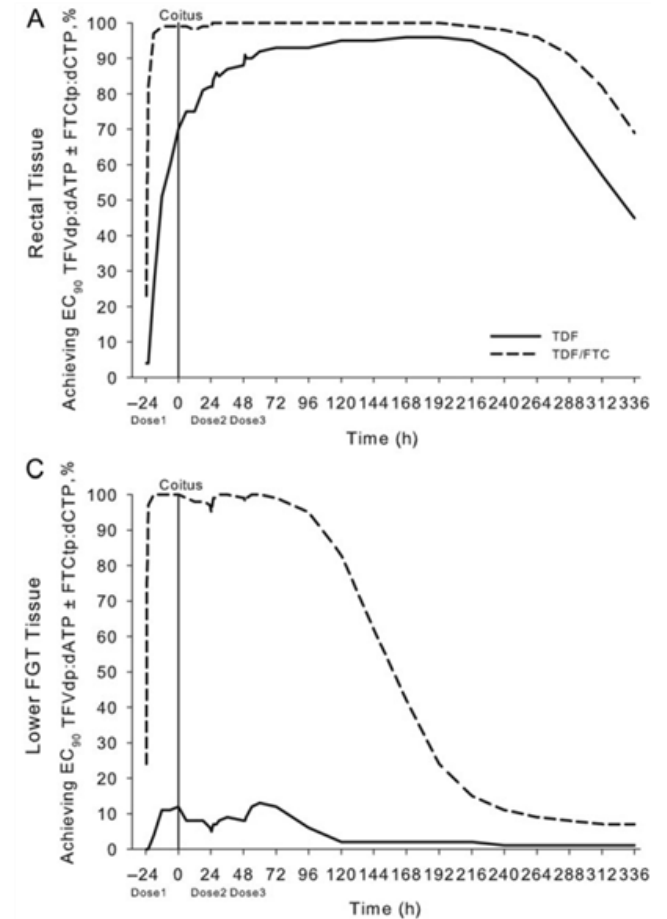
Individual Likert-scale items for each modality ^a	n	Mean (SD)	Median (IQR ^b)	Mode	<i>P</i> -value ^c
Daily oral pill	1036	3.31 (1.4)	4 (2)	4	Reference
On-demand pills ^d	1105	3.63 (1.4)	4 (2)	5	<.001
Injection ^e	1091	3.27 (1.5)	4 (3)	5	.02
Penile gel before intercourse	755	3.45 (1.4)	4 (3)	5	.001
Penile gel after intercourse	751	3.31 (1.5)	4 (3)	5	.28
Rectal gel before intercourse	791	3.06 (1.5)	3 (2)	4	<.001
Rectal gel after intercourse	794	3.00 (1.5)	3 (2)	1	<.001
Rectal suppository before intercourse	792	2.58 (1.4)	2 (3)	1	<.001
Rectal suppository after intercourse	791	2.90 (1.5)	3 (3)	1	<.001

^aThe 5-point Likert-scale items where 1=very unlikely, 2=somewhat unlikely, 3=neither likely or unlikely, 4=somewhat likely, 5=very likely.

(Hall, JMIR, 2016)

How much PrEP is enough PrEP?

- Beyond the issue of habits is pharmacokinetics
- On demand PrEP may be sufficient for HIV protection in rectal tissue, but not vaginal
- Simulation of the IPERGAY regimen
 - >95% achieved target exposure (EC_{90}) in female genital tract tissue through 72 hours
 - <85% were at target exposure by 120 hours
- A minimum of 6 doses per week was required to protect female genital tract tissue from HIV



(Cottrell, JID, 2016)

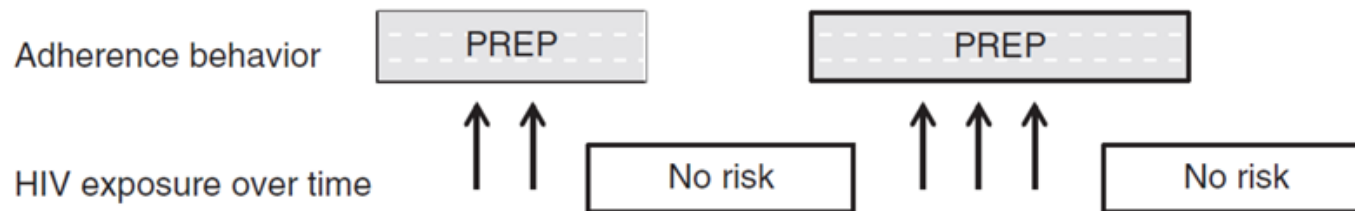
Implications for different populations

- On demand PrEP may be a good option for MSM who want it and are motivated by sex as a cue for adherence
- Women likely need 6/7 doses per week to prevent vaginal transmission, making on demand PrEP a poor option for this population
- We have no idea what to recommend for men who have sex with women

Prevention-effective adherence

- Prevention-effective adherence: alignment of adherence and risk for HIV acquisition (*Haberer, AIDS, 2015*)

Prevention-effective adherence paradigm: 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.



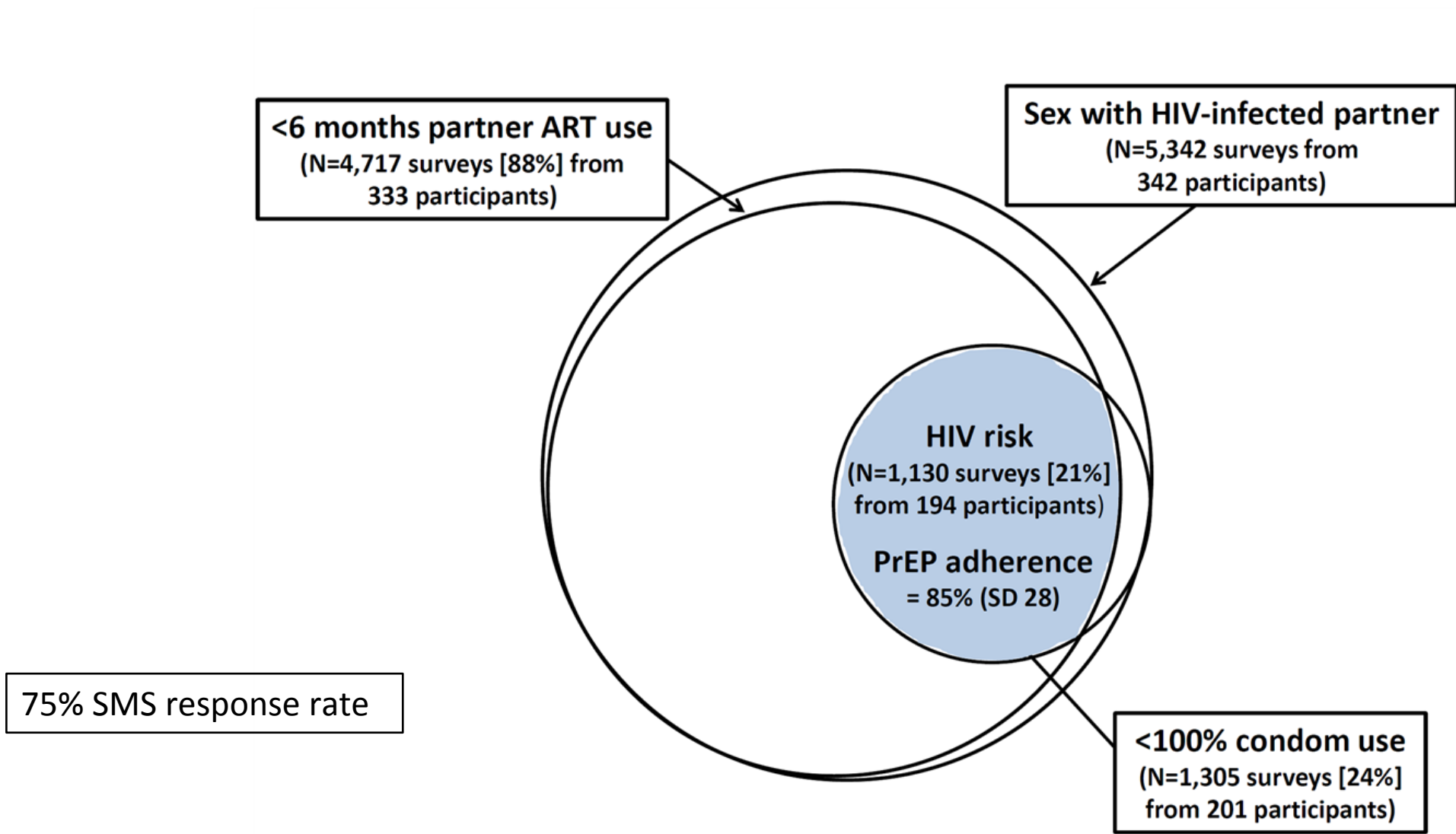
- The key is knowing when HIV risk is present

Measuring prevention-effective adherence

- Sex and associated behavior (e.g., condom use) are difficult to measure
- Self-report of these behaviors is limited by recall and social desirability bias (*Catania, Psychol Bull. 1990*)
- Measurement approaches
 - Time-line follow-back (IAVI pilot RCT of intermittent PrEP)
 - SMS/calls (IAVI, Partners Demonstration Project, HPTN067/ADAPT)
 - Diaries



Enrollment		Months						
0		1	2	3	4	5	6	etc.
PrEP given (1 month)		PrEP given (3 month)				PrEP given (3 month)		
Survey training period	SMS survey				SMS survey			SMS survey



(Haberer, IAPAC, 2016)

Prevention-effective adherence for each approach

- On demand...
 - Assessment on a day-to-day basis
 - Requires a commitment to the adherence cue of sex
 - Unique potential barriers: unanticipated sex
- Daily...
 - Assessment by the “season”
 - Requires a commitment to a daily routine
 - Unique potential barriers: pill taking fatigue, taking PrEP when not having sex



NYC Play Sure Kit

Parting thoughts

- On demand PrEP is a good option for MSM, but choice is important
- Counseling messages for either on demand or daily PrEP need to address common adherence barriers (e.g., risk perception, stigma, logistics) and means for developing good habits
- Monitoring for accurate use of on demand PrEP is challenging and an open area for further research

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