

# Pre-exposure Prophylaxis for HIV Prevention

## Concerns about PrEP: Adherence

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# Topics To Be Covered

- The importance of adherence to PrEP (review)
- How to monitor adherence to PrEP
- How to promote adherence to PrEP
- What about intermittent dosing strategies....?

## Key HIV PrEP Trials Using Oral Tenofovir (TDF) or Tenofovir-Emtricitabine (TDF-FTC)

Study	Study Population	Study Randomization	HIV Incidence Impact
<b>IPrEx</b> (Brazil, Ecuador, South Africa, Thailand, US)	2499 MSM and transgender women	Daily oral TDF-FTC or placebo	TDF-FTC: 44% ↓
<b>Partners PrEP Study</b> (Kenya, Uganda)	4147 heterosexual HIV discordant couples	Daily oral TDF, TDF-FTC, or placebo	TDF: 67% ↓ TDF-FTC: 75% ↓
<b>TDF2 Study</b> (Botswana)	1219 heterosexual men and women	Daily oral TDF-FTC or placebo	TDF-FTC: 63% ↓
<b>FEM-PrEP</b> (Kenya, South Africa, Tanzania)	2120 women	Daily oral TDF-FTC or placebo	TDF-FTC: no protection
<b>VOICE</b> (South Africa, Uganda, Zimbabwe)	5029 women	Randomized to daily oral TDF, TDF-FTC, oral placebo, TDF vaginal gel, or gel placebo	TDF: no protection TDF-FTC: no protection TDF gel: no protection
<b>Bangkok TDF Study</b> (Thailand)	2413 injection drug users	Randomized to daily oral TDF or placebo	TDF: 49% ↓
<b>IPERGAY</b> (France, Quebec)	400 MSM	Randomized to “on-demand” TDF-FTC or placebo	TDF-FTC: 86% ↓
<b>PROUD</b> (United Kingdom)	545 MSM and transgender women	Randomized to daily oral TDF-FTC immediately or delayed	Immediate TDF-FTC: 86% ↓

# The Relationship Between Adherence and Efficacy

	<b>Efficacy in randomized comparison</b>	<b>% of blood samples with tenofovir detected</b>
<b>Partners PrEP</b>	75%	81%
<b>TDF2</b>	62%	79%
<b>Bangkok TDF</b>	49%	67%
<b>iPrEx</b>	44%	51%
<b>FEM-PrEP</b>	6%	26%
<b>VOICE</b>	-	29%

Baeten et al N Engl J Med 2012  
Grant et al N Engl J Med 2010  
Choopanya et al Lancet 2013

Van Damme et al N Engl J Med 2012  
Thigpen et al N Engl J Med 2012  
Marrazzo et al CROI 2013 #26LB

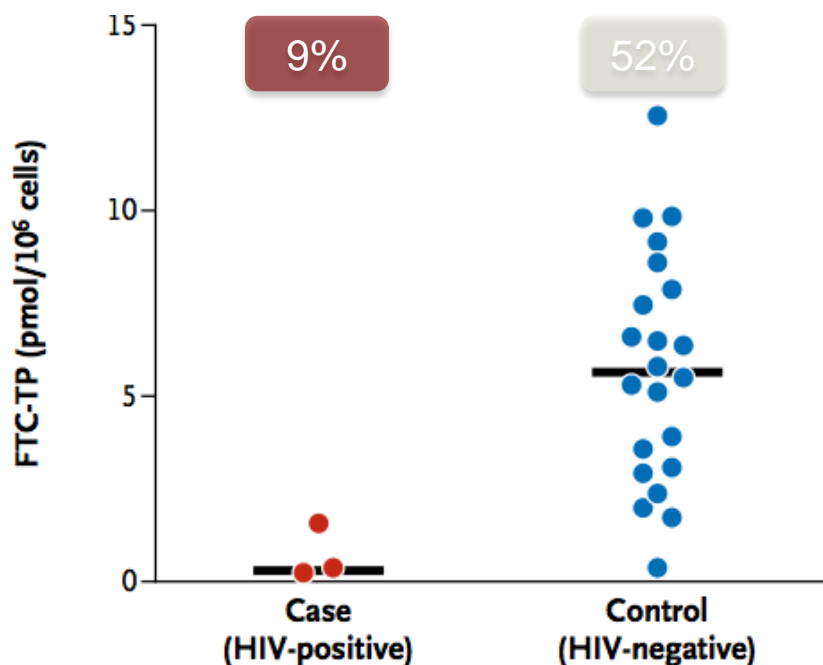
# Preexposure Prophylaxis (PrEP) for HIV Prevention in MSM

## iPrEx Trial: Results

### Detectable Drug Levels in Patients on Tenofovir-Emtricitabine

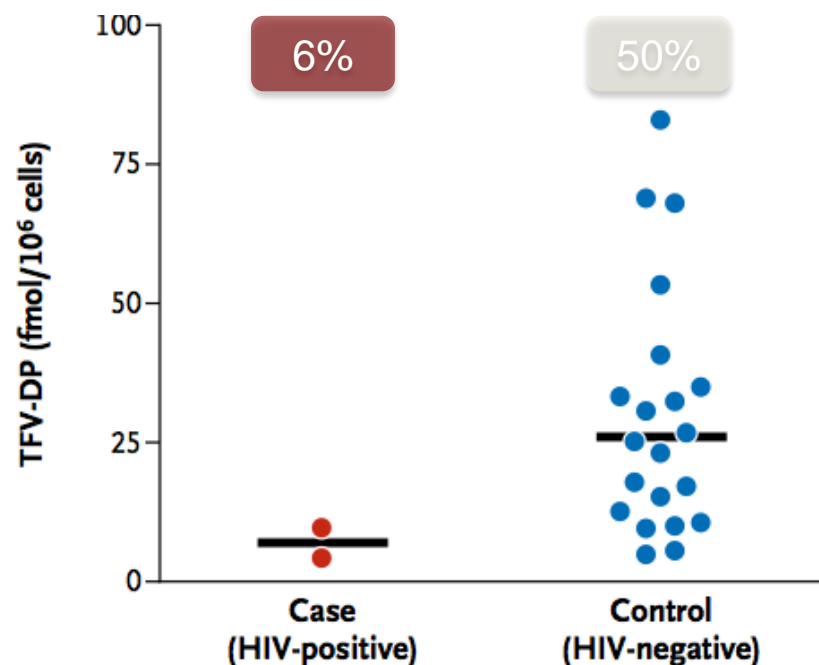
#### A. Intracellular Emtricitabine Levels

##### A Intracellular FTC-TP Level



#### B. Intracellular Tenofovir-DF Levels

##### B Intracellular TFV-DP Level



**Adjusted RR reduction (any detectable level) = 95%**

# Adherence and Efficacy in Open-label Projects

- iPrEx OLE (open label extension)

Grant et al., Lancet, 2014  
adherence 71%

Estimated adherence (TDF in DBS)	Incidence
Not detected	4.7/100 person-years
<2 tab/week	2.3/100 person-years
2-3 tab/week	0.6/100 person-years
4-7 tab/week	0/100 person-years

- San Francisco, Miami, D.C

Liu et al., JAMA Intern Med, 2016

adherence 80-86%

2 infections (incidence 0.43/100py)

# Recommended Follow-Up Counseling and Services

## Recommended Follow-Up Counseling and Services for Patients Taking PrEP

### Follow-up services

Every 3 months

Adherence counseling

✓

Behavioral risk reduction support and condoms

✓

Assessment for side effects

✓

Assessment for STI symptoms and symptoms of acute HIV

✓

For women, discuss pregnancy intent and contraceptive options

✓

Access to clean needles/syringes and drug treatment services

✓

Provide a refill of daily TDF/FTC for no more than 90 days

✓

Abbreviations: STI = sexually transmitted infection; TDF/FTC = tenofovir/emtricitabine

# How to Monitor Adherence to PrEP

## Lessons from iPrEx

- 510 subjects with plasma levels drawn at wk 24

	Self-report	CASI	Pharmacy data
100%	55%	43%	65%
90-99%	22%	29%	22%
50-89%	13%	18%	10%
<50%	2%	2%	3%
Missing/unknown	7%	9%	

- Among subjects reporting 100% adherence
  - 51% had any drug detected
  - 35% had levels consistent w regular dosing



# THE DEMO PROJECT



## Adherence, Sexual Behavior and HIV/STI Incidence Among MSM and Transgender Women in the US PrEP Demo Project

A Liu, S Cohen, E Vittinghoff, P Anderson, S Doblecki-Lewis, O Bacon, W Chege, R Elion, S Buchbinder, M Kolber

***8<sup>th</sup> IAS Conference on HIV Pathogenesis, Treatment, and Prevention  
Vancouver, Canada***

The views expressed herein do not necessarily reflect the official policies of the City and County of San Francisco; nor does mention of the San Francisco Department of Public Health imply its endorsement. Slides courtesy of Albert Liufdf

# Demo Project Sites

San Francisco City Clinic  
(N=300)



Miami-Dade County  
Downtown STD clinic  
(N=157)



Whitman Walker Health  
(N=100)



- Annual HIV seroconversion rate among MSM >2% across clinics
- Participants were either clinic referred (46%) or self-referred (54%)

# The Demo Project Methods: (cont'd)

- PrEP adherence (all visits)
  - Self-reported adherence rating scale
  - Medication possession ratio (pills dispensed/total days between visits)
  - Dried blood spots for tenofovir diphosphate (TFV-DP)
    - Random sample of ~100 participants/site tested\*
    - Protective TFV-DP levels associated with  $\geq 700$  fmol/punch ( $\geq 4$  doses/week)<sup>1,2</sup>
- PrEP engagement: 5-level ordinal measure

TFV-DP (fmol/punch)	Adherence Interpretation
700	$\geq 4$ doses/week
350 to 699	2-3 doses/week
<350	< 2 doses/week
BLQ	No recent dosing
Missed visit	Missed visit

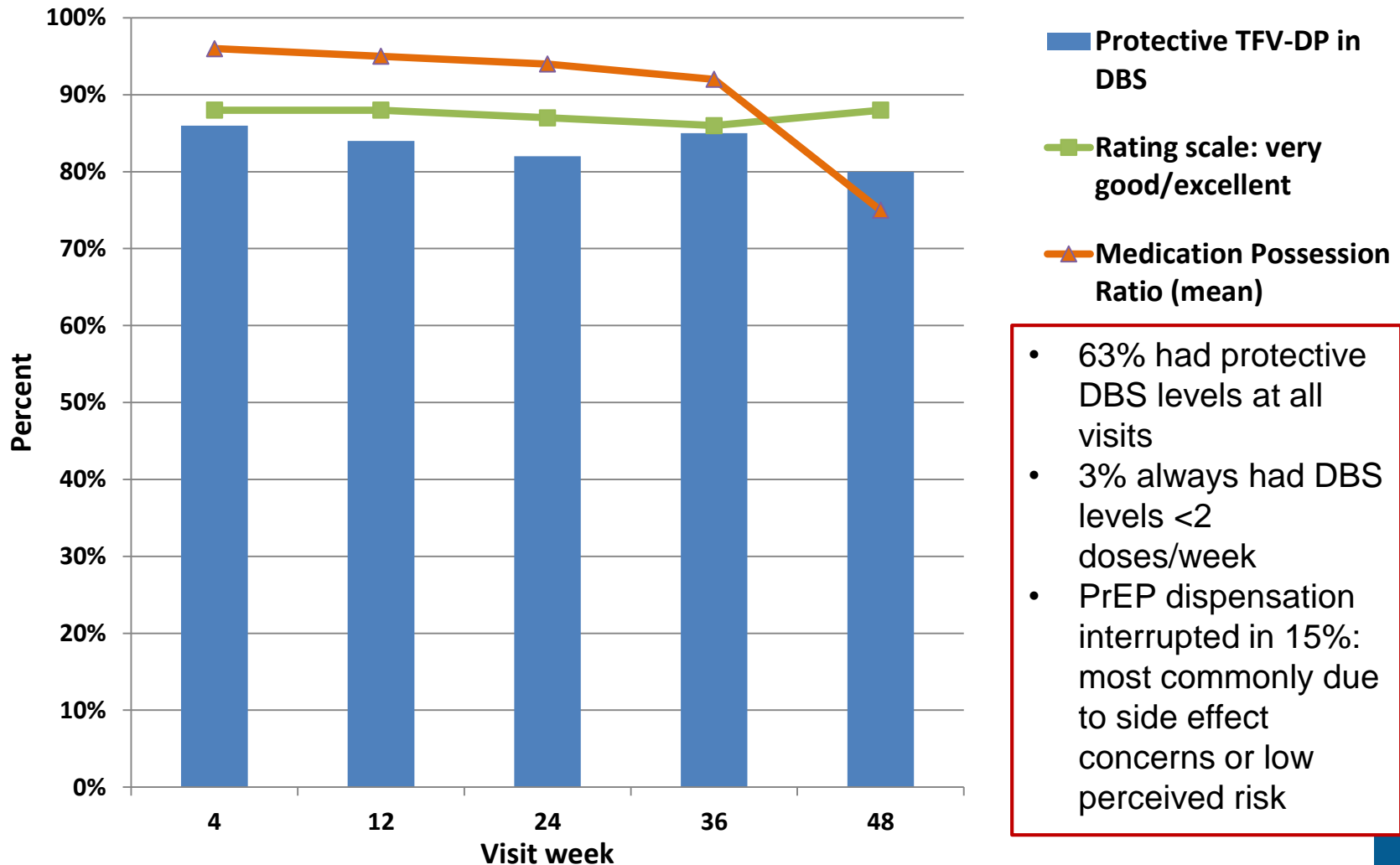


- Adherence & sexual/drug behaviors evaluated using GEE & Poisson models

<sup>1</sup>Grant Lancet ID 2014; <sup>2</sup>Castillo-Mancilla et al. AIDS Res Hum Retroviruses 2013

\*DBS from all Black and transgender ppts tested; results weighted to reflect overall cohort

# The Demo Project Results: Adherence



# The Demo Project:

## Independent predictors of protective DBS levels

Characteristic	% PL*	AOR (95% CI)	P value
Site			
San Francisco	90	Ref	
Miami	65	<b>0.32 (0.17-0.60)</b>	<b>&lt;0.001</b>
DC	88	1.08 (0.54-2.19)	0.82
Race/Ethnicity			
White	91	Ref	
Latino	77	0.81 (0.41-1.61)	0.55
Black	57	<b>0.28 (0.12-0.64)</b>	<b>0.003</b>
Asian	84	0.72 (0.17-3.03)	0.65
Other	82	0.42 (0.13-1.38)	0.15
Living situation			
Rent or own housing	87	<b>2.02 (1.14-3.55)</b>	<b>0.02</b>
Other	70	Reference	
# condomless anal sex partners, past 3 mo			
0-1	75	Reference	
≥2	89	<b>1.82 (1.14-2.89)</b>	<b>0.01</b>

\*PL = Protective DBS levels (TFV-DP in DBS consistent with ≥4 doses/week)

OR for protective levels did not differ by age, education, alcohol, or drug use

# How to Monitor Adherence to PrEP

- 1) Does your patient show up to appointments?
- 2) Did your patient pick up their prescriptions?
- 3) Single best questions
  - How many pills missed in the last month?
  - How many pills missed in the last week?
  - How good has your adherence been over the last month?  
(very poor, poor, fair, good, very good, excellent)

# How to Promote Adherence to PrEP

- At baseline
  - Provide education about PrEP
    - Importance of adherence, side effects
  - Help to establish a dosing routine
    - What to do about missed doses
  - Discuss reminder systems and tools
  - Address financial, substance abuse, mental health needs
  - Facilitate social support
- During follow-up
  - Assess adherence and identify barriers to adherence
  - Assess and help manage side-effects
  - Normalize missed doses
  - Reinforce success

# Reminder Systems and Adherence Tools

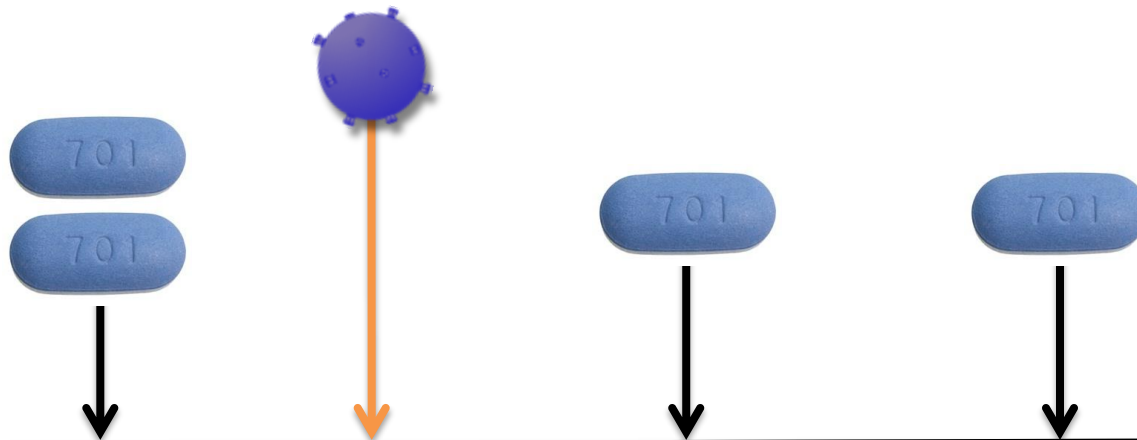
- Medisets
- Alarms and reminders
  - Old school alarm clocks
  - Phones
  - Smartwatches
- Text messaging/emails
- Apps
- MedMinder (\$40-60/month)





# Intermittent or “On-Demand” Preexposure Prophylaxis IPERGAY Event-Driven Strategy

HIV Exposure Event

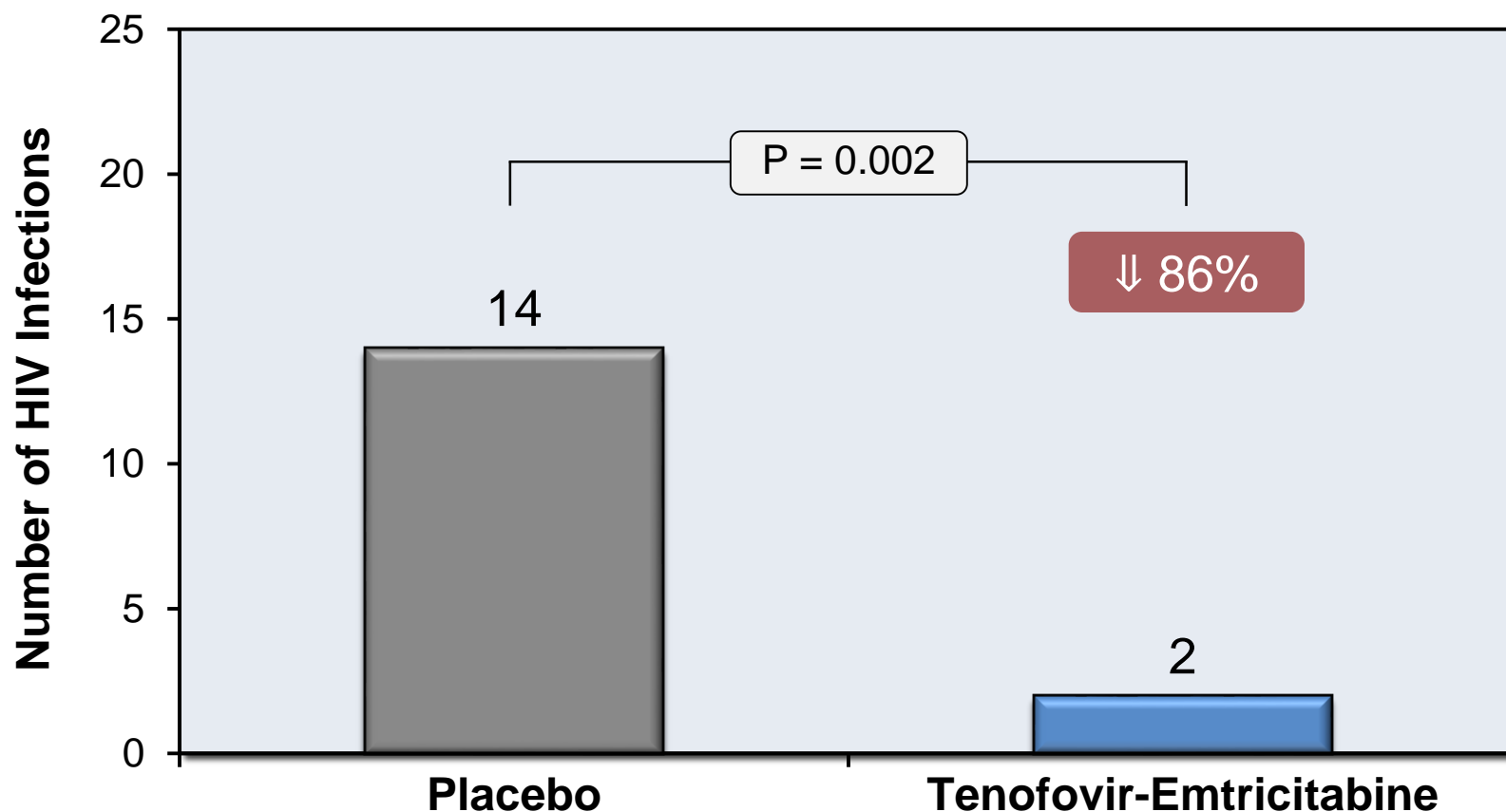


2 tabs 2-24 hours before sex  
(or 1 pill if most recent dose  
taken between 1-6 days prior)

1 tab 24 and 48  
hours after the last  
pre-sex dose

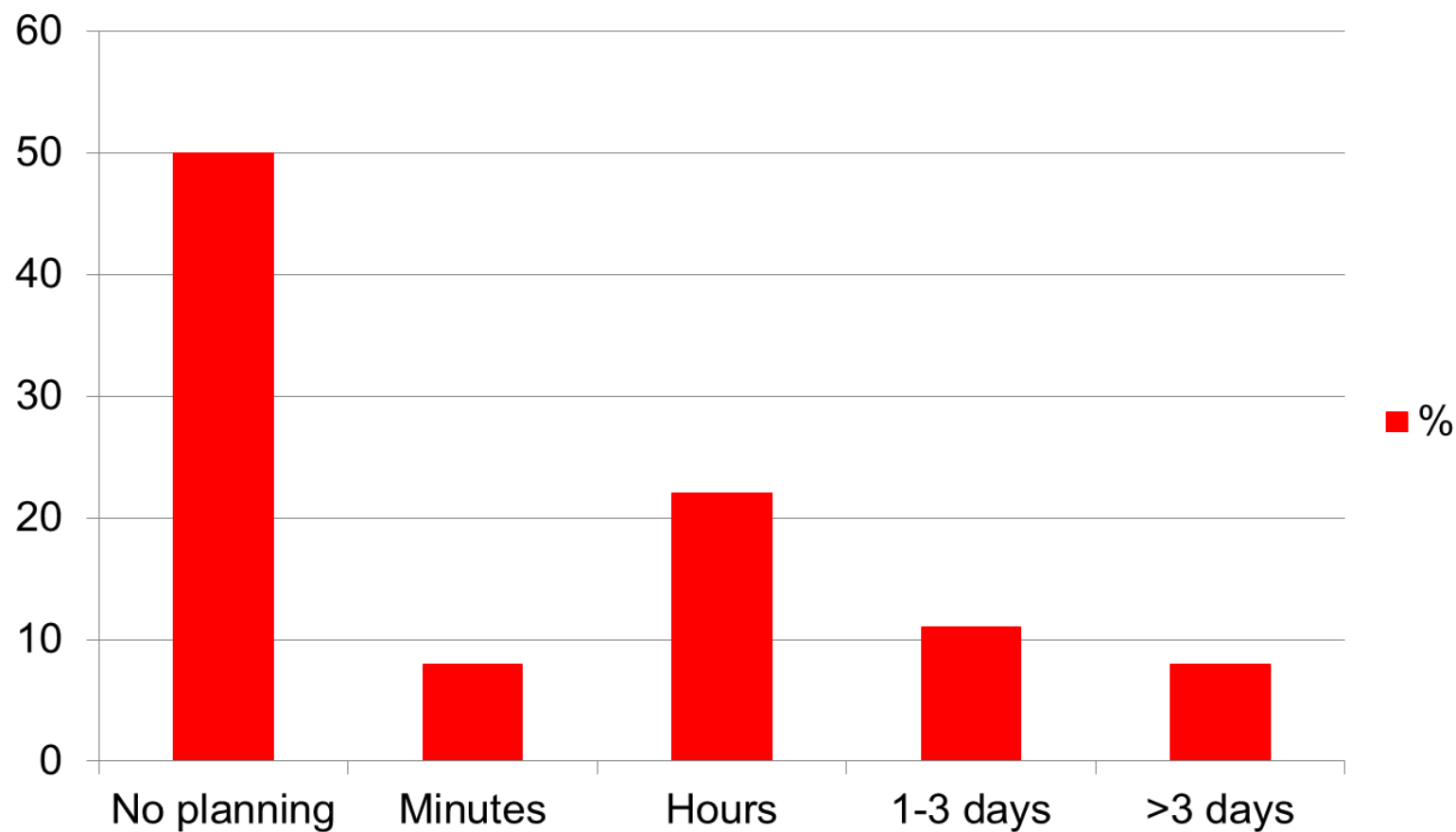
# Intermittent or “On-Demand” PrEP for High-Risk MSM

## IPEGAY: Results



Due to high effectiveness of PrEP, participants unrandomized and all offered PrEP

# How far in advance do MSM “plan” for sex?



N=1013

Volk et al, JAIDS, 2012

US Public Health Service

# PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE



Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline Page 1 of 67

[www.cdc.gov/hiv/pdf/prepguidelines2014.pdf](http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf)

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline Page 1 of 67

Source: US Public Health Service. Clinical practice guidelines for PrEP. May 2014.

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