

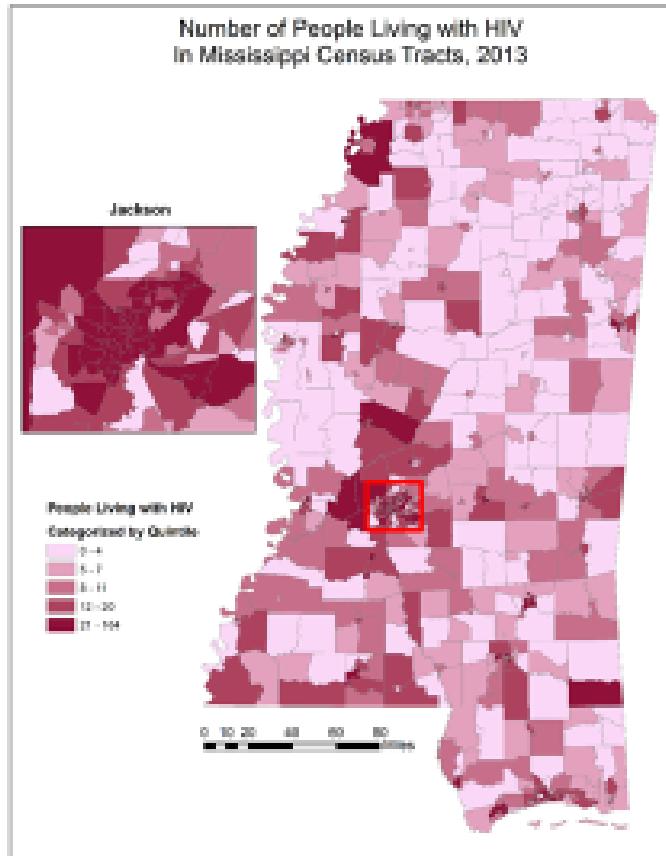
# PrE-Exposure Prophylaxis (**PrEP**)

## A “New” Tool to Fight HIV



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Assistant Professor  
Division of Infectious Diseases  
University of Mississippi Medical Center

# HIV/AIDS in Mississippi



- **Mississippi ranked 7th in the nation for HIV/AIDS prevalence in 2013**
  - 76% of the new HIV cases documented in 2013 were African-American with diagnosis rates 8 times higher than Whites.
- **Jackson had the 7<sup>th</sup> highest HIV and 2<sup>nd</sup> highest AIDS diagnosis rates in 2013** of any US metropolitan statistical area (MSA) with a population 500,000 or greater
  - Nearly one-half of new HIV diagnoses in 2011 in Jackson were among African-American MSM
- **Between 2009-2011 HIV incidence increased 171% among 13-24 years old**

Sources: 2013 MSDH STD/HIV Surveillance; CDC 2013 HIV Surveillance Report

# Potential Intervention Approaches to Prevent HIV Transmission

## Decrease Source of HIV Infection

- Barrier protection
- STI treatment
- Blood screening
- ART
  - Maternal-to-child transmission
  - Decrease partner's viral load
  - Treatment of acute HIV infection

## Decrease Host Susceptibility to HIV Infection

- **Barrier protection**
- **STI treatment**
- **PEP**
- **PrEP**
- **Topical microbicides**
- **Vaccines**
- **Infection control**
- **Circumcision**

## Alter Risk-Taking Behavior

- **Condom promotion**
- **Individual intervention**
- **Couples intervention**
- **Community based intervention**
- **Structural intervention**

# **PrEP Rationale**

**Having HIV drugs present at the site of exposure should reduce the risk of infection.**

# Indication: TRUVADA for PrEP

- TRUVADA is indicated in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in adults at high risk
- This indication is based on clinical trials in Men who have sex with Men (MSM) and in heterosexual serodiscordant couples at high risk for HIV-1 infection
- TRUVADA for PrEP requires taking one pill, once daily



Pill image is for illustration only; not actual size.

# PrEP: Efficacy Rates in Clinical Trials

iPrEx (TDF/FTC)	FEM-PrEP (TDF/FTC)	TDF2 (TDF/FTC)
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The NEW ENGLAND JOURNAL of MEDICINE

*The NEW ENGLAND JOURNAL of MEDICINE*

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## Tenofovir-Based Preexposure Prophylaxis for HIV Infection among African Women

Jeanne M. Marrazzo, M.D., Gita Ramjee, Ph.D., Barbra A. Richardson, Ph.D., Kailazarid Gomez, M.P.A., Nyaradzo Mgodzi, M.Med., Gonasagrie Nair, M.B., Ch.B., M.P.H., Thesla Palanee, Ph.D., Clemensia Nakabiito, M.Med., Ariane van der Straten, Ph.D., Lisa Noguchi, M.S.N., Craig W. Hendrix, M.D., James Y. Dai, Ph.D., Shayhana Ganesh, M.Med., Banningi Mkhize, M.B., Ch.B., Marthinette Taljaard, B.S., Urvi M. Parikh, Ph.D., Jeanna Piper, M.D., Benoît Mâsse, Ph.D., Cynthia Grossman, Ph.D., James Rooney, M.D., Jill L. Schwartz, M.D., Heather Watts, M.D., Mark A. Marzinke, Ph.D., Sharon L. Hillier, Ph.D., Ian M. McGowan, M.D., and Z. Mike Chirenje, M.D., for the VOICE Study Team\*

Timothy D. Mastro, M.D., and Douglas Taylor, Ph.D., for the FEM-PrEP Study Group\*

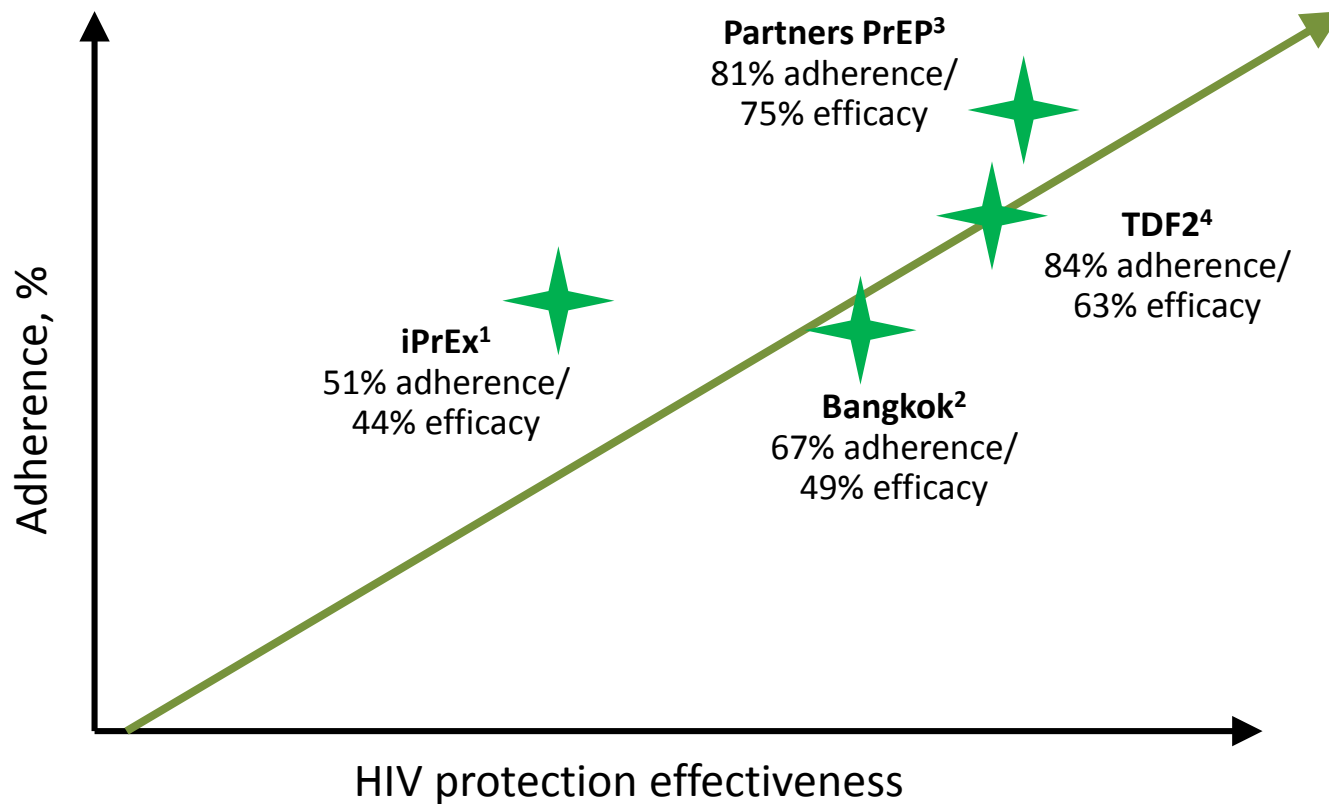
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# PrEP: Results from Clinical Trials

Clinical trial	Participants	Number	Drug	mITT <sup>a</sup> efficacy of % reduction in acquisition of HIV infection <sup>b</sup>		Adherence adjusted efficacy based on TDF detection in blood <sup>c</sup>	
				%	(95% CI)	%	(95% CI)
<b>iPrEx</b>	Men who have sex with men (MSM)	2499	TVD	42	(15-63)	<b>92</b>	(40-99)
<b>Partners PrEP</b>	HIV discordant couples	4747	TDF	67	(44-81)	<b>86</b>	(67-94)
			TVD	75	(55-87)	<b>90</b>	(58-98)
<b>TDF 2</b>	Heterosexually active men and women	1200	TVD	63	(22-83)	<b>85<sup>d</sup></b>	NS
<b>Bangkok Tenofovir Study</b>	IDU	2413	TDF	49	(10-72)	<b>74</b>	(17-94)
<b>Fem-PrEP</b>	Heterosexually active women	1951	TVD	NR	-----	<b>NR</b>	-----
<b>VOICE</b>	Heterosexually active women	5029	TVD	NR	-----	<b>NR</b>	-----

- a. Modified Intent to Treat
- b. Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
- c. The percentage of reduction in HIV incidence among those with TFV detected in blood, compared with those without detectable TFV
- d. Finding not statistically significant

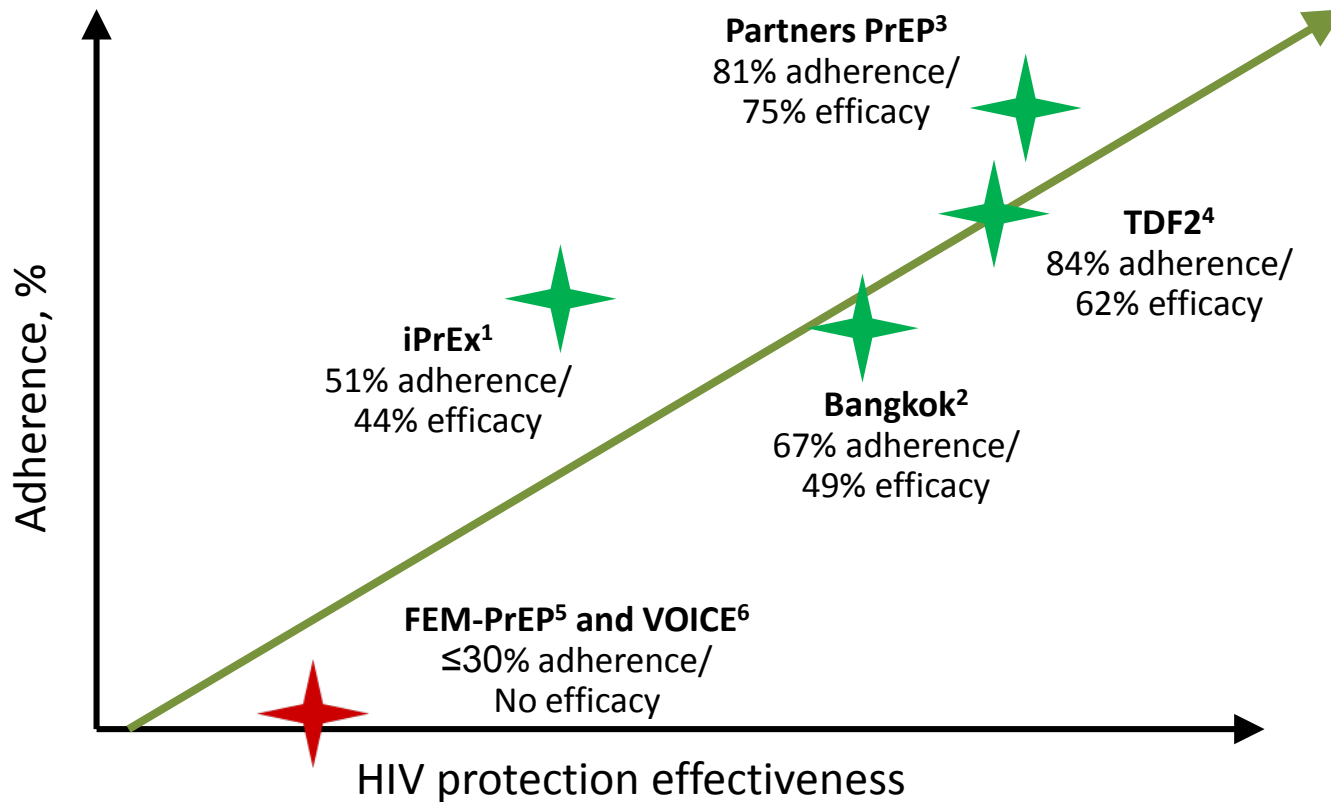
# PrEP: Better Adherence Correlates with Higher Efficacy



**Trials where the majority of subjects were adherent demonstrated HIV protection, with higher protection estimates when more of the population was adherent**



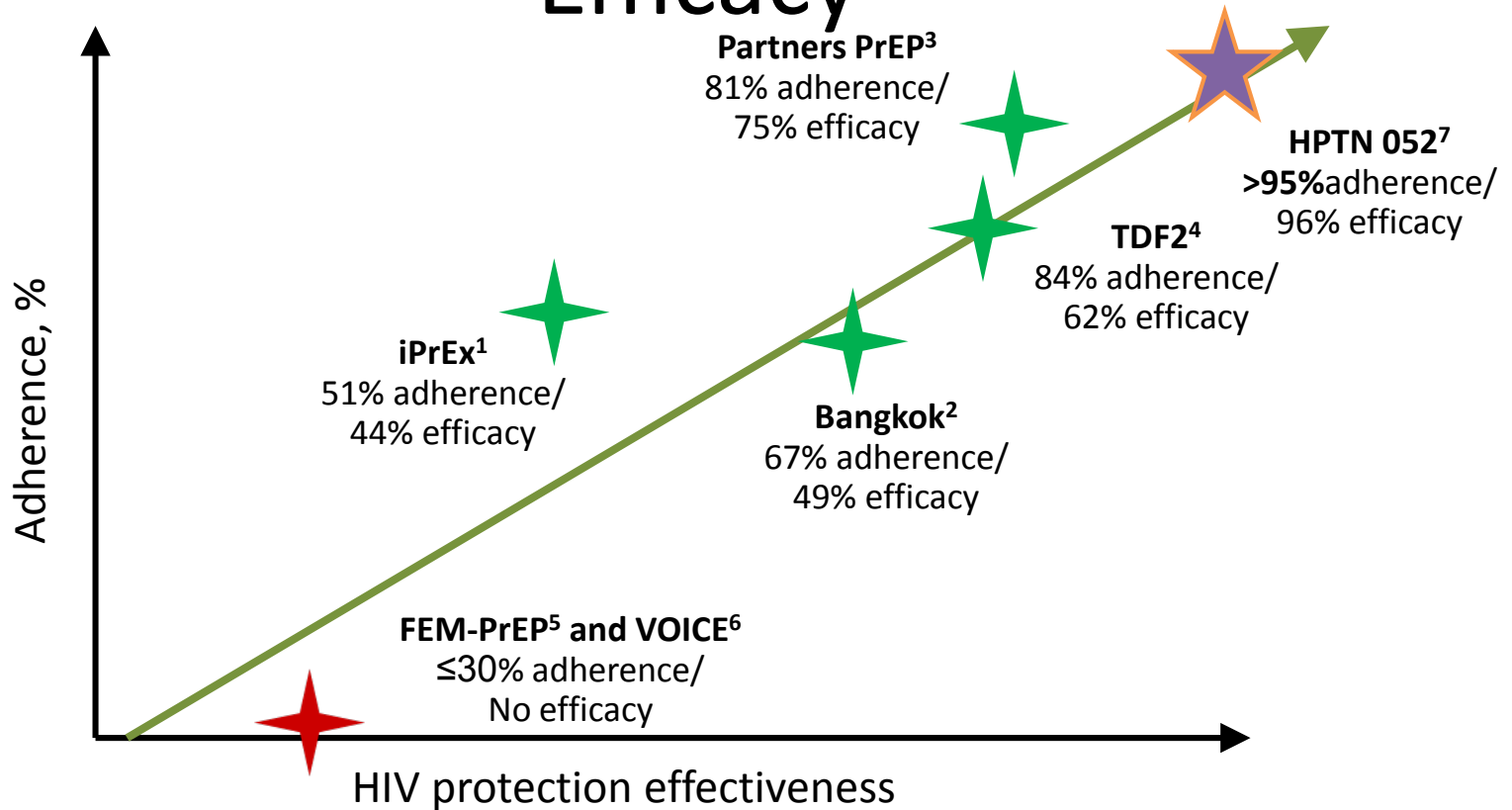
# PrEP: Low Adherence Correlates with Poor Efficacy



**Trials where only a minority of subjects were adherent did not/could not demonstrate HIV protection**

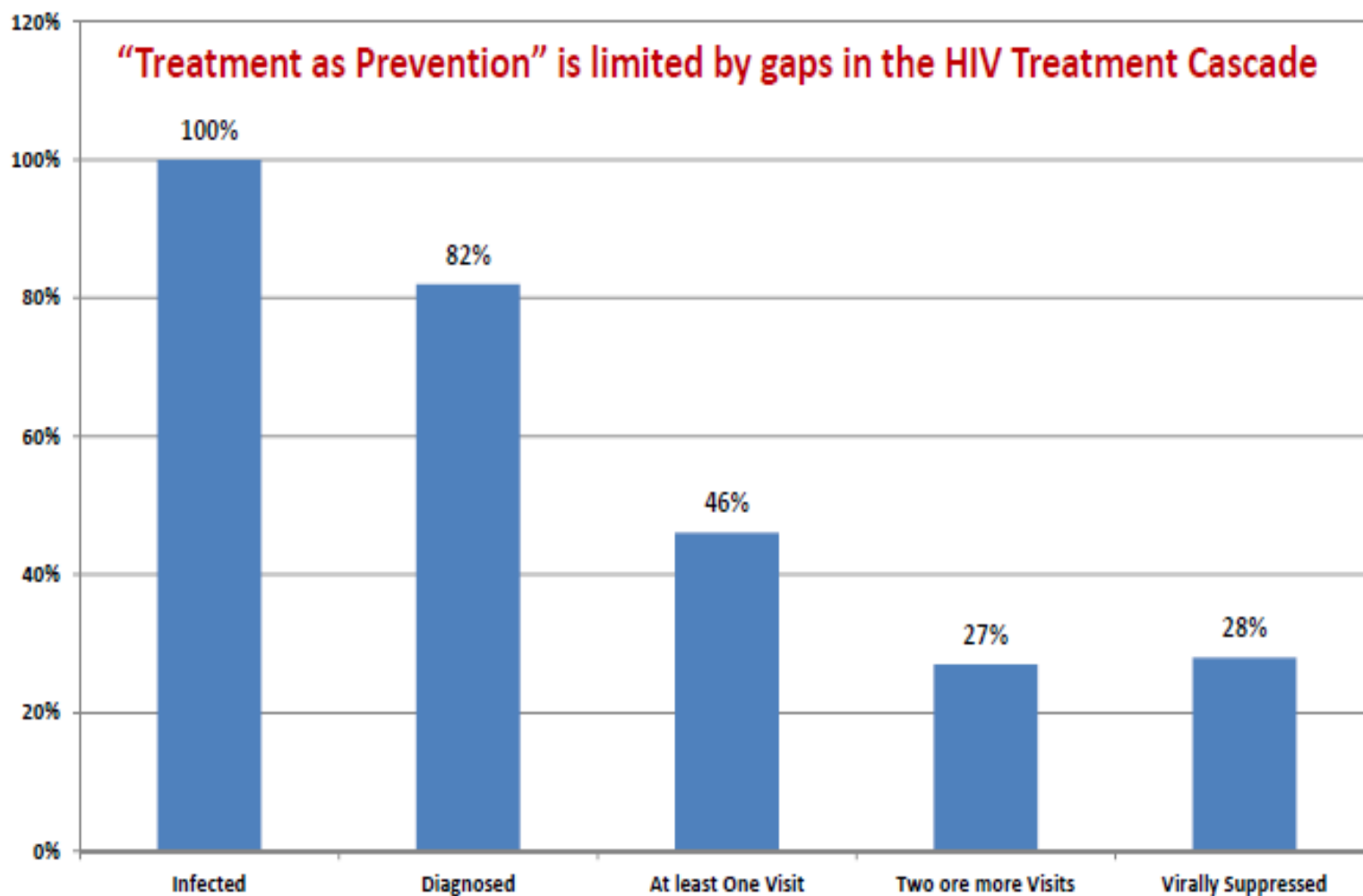
1. Grant R, et al. *N Engl J Med* 2010;363:2587-99. 2. Choopanya K, et al. *The Lancet*. June 13, 2013. 3. Baeten J, et al. *N Engl J Med* 2012;367:399-410. 4. Thigpen M, et al. *N Engl J Med* 2012;367:423-34. 5. Van Damme L, et al. *N Engl J Med* 2012;367:411-22. 6. Van der Straten A, et al. *AIDS* 2012;26(7):F13-F19

# Treatment as Prevention (TasP): Better Adherence Correlates with Higher Efficacy



**HPTN 052 showed that suppressive ART, from very high adherence, nearly eliminated HIV transmission risk**

## Mississippi Continuum of Care, overall population Diagnosed in 2012 and living through 2013



# PrEP Protection by the Numbers

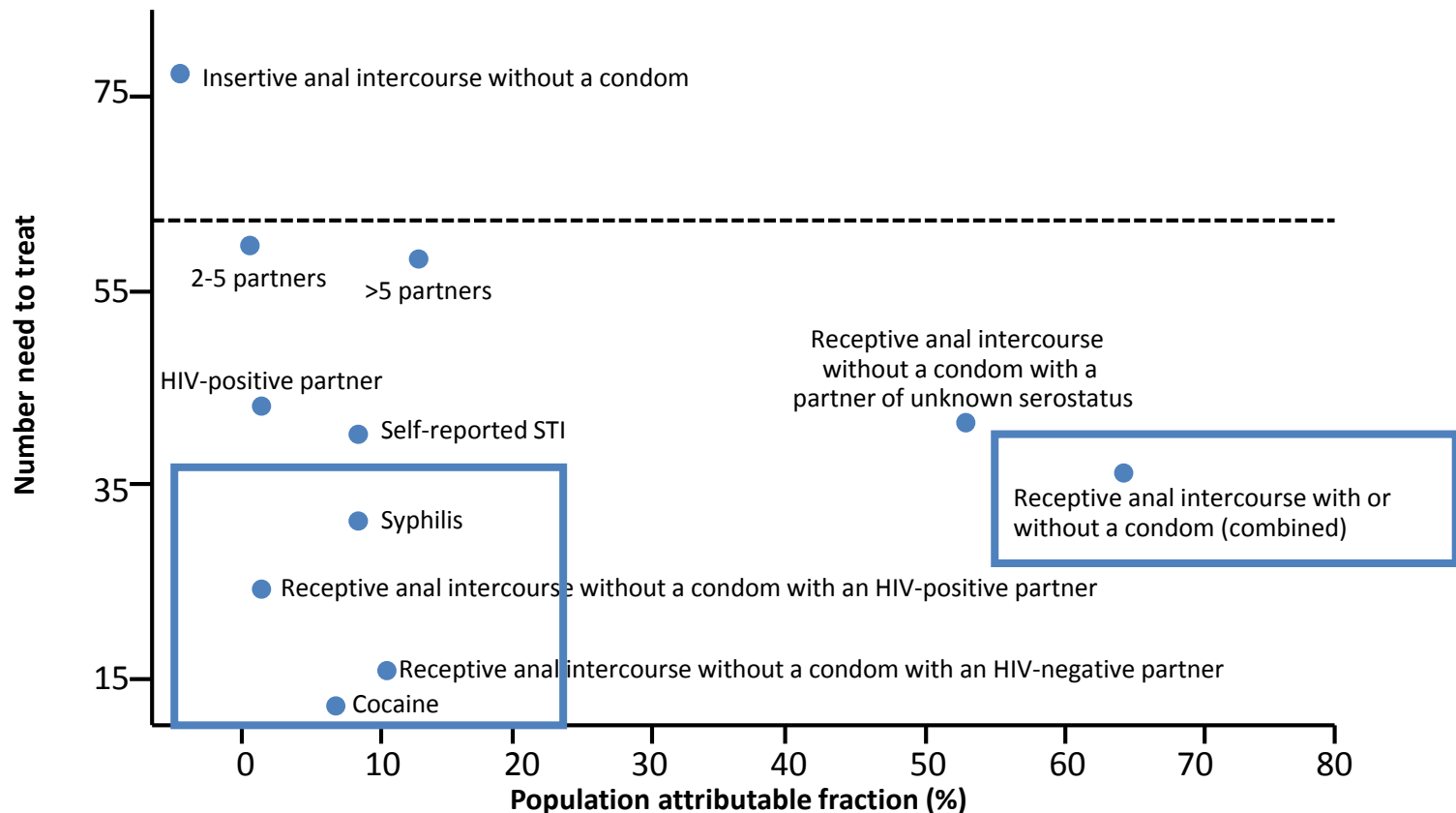
## Context Matters

- **44%** efficacy seen with primary iPrEX analysis
- **92%** efficacy among the 51% of iPrEX pts who had drug detected in their systems
- **99%** protection based on modeling drug levels if drug taken every day
- **100%** of iPrEX open label participants did not get infected if their drug levels were c/w taking PrEP  $\geq 4$  X a week





# Quantifying Individual and Public Health Benefits of PrEP



**The largest PAF was for men who had RAI without a condom, regardless of HIV status of partners (HIV+, “HIV-”, or HIV-unknown).  
Even in this group, the number needed to treat was only 36**

# PrEP clinical questions

**Symptoms: Start-up, GI, uncommon**

**Renal: uncommon with monitoring**

**Bone: some decrease BMD, no pathologic fractures**

**Selection for resistance: rare, almost all 184V**

**Risk compensation vs. reaching those at risk**

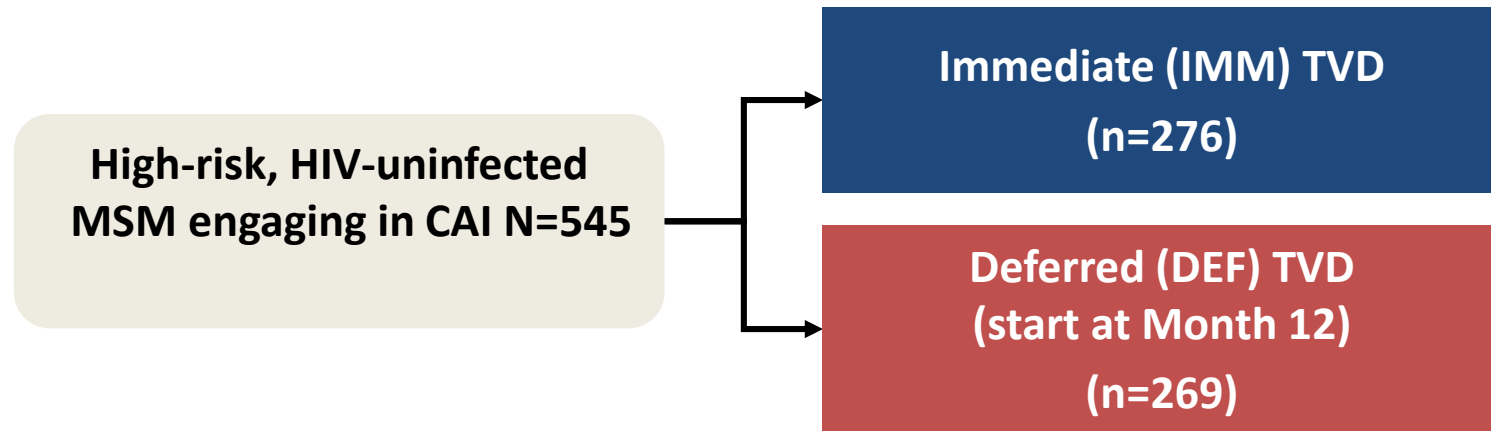
**Other STI: need for frequent monitoring; HSV-2?**

**Other approaches: microbicides, immunoprophylaxis**

# PROUD: Pragmatic Open-Label Randomized Trial of Pre-Exposure Prophylaxis

## Study Design/Results

Randomized, multicenter, open-label pilot study in the UK



**86% (90% CI: 58%-96%) Risk Reduction;  $P=0.0002$**

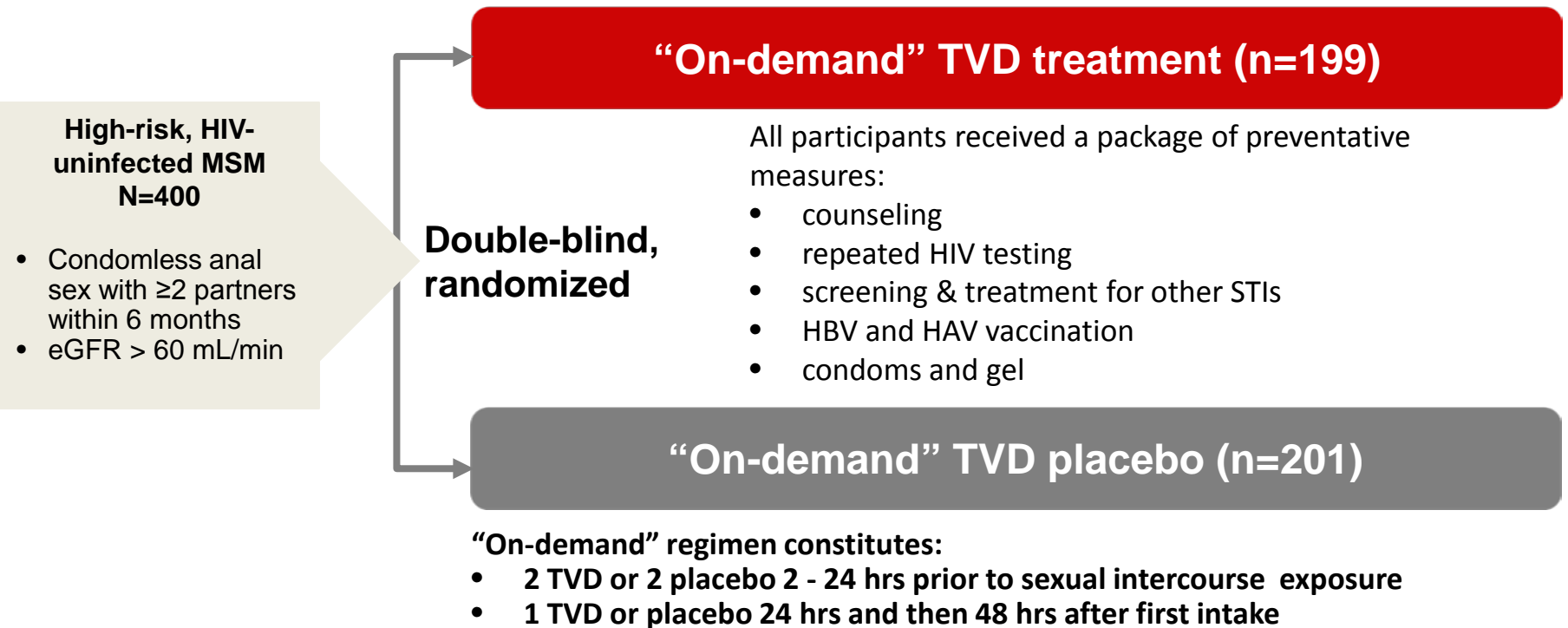
**Number needed to treat=13 (90% CI: 9-25)**

CAI, condomless anal intercourse

All subjects received comprehensive HIV prevention services, including condoms, risk-reduction counseling, testing and treatment for sexually transmitted infections, and HIV pre- and post-test counseling

# IPIRGAY: On-Demand PrEP

## Study Design



**Primary endpoint:** HIV seroconversion

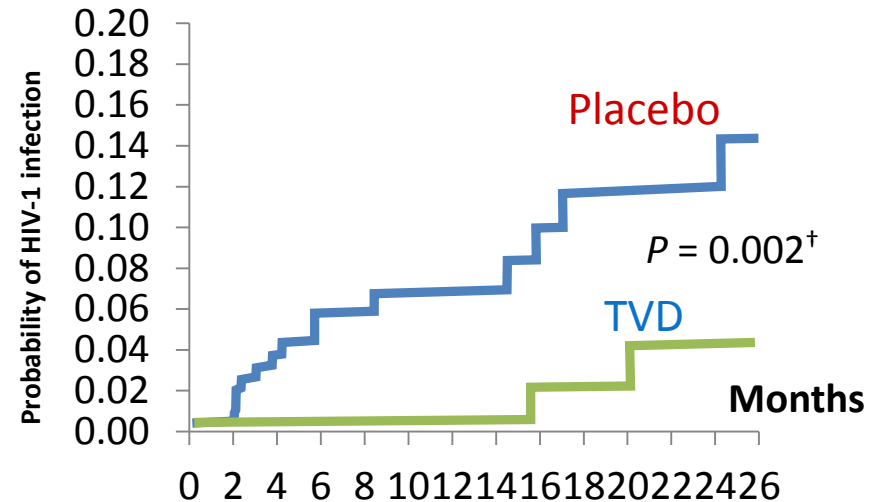
**Secondary endpoints:** Sexual behavior, safety events, adherence



# IPERGAY: On-Demand PrEP

## Results: Efficacy\*

- **16 subjects infected**
  - **PBO=14** (incidence: 6.6/100 PY)
  - **TVD=2** (incidence: 0.94/100 PY)
- Average 16 pills / month
- Average 2 sexual encounters a week
- Number needed to treated: **18**  
for 1 year to prevent 1 HIV infection



Placebo, n	201	141	74	55	41
TVD, n	199	140	82	58	43

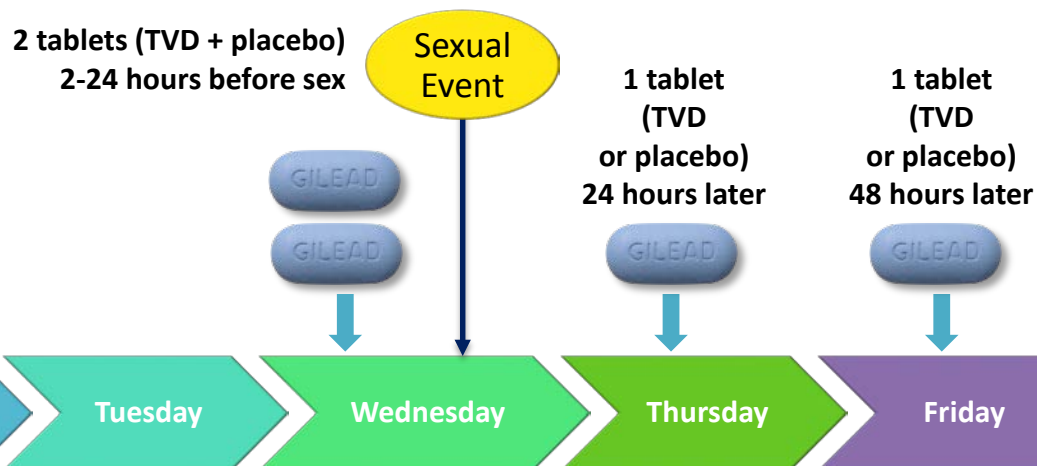
\*mITT Population

†Log-rank test

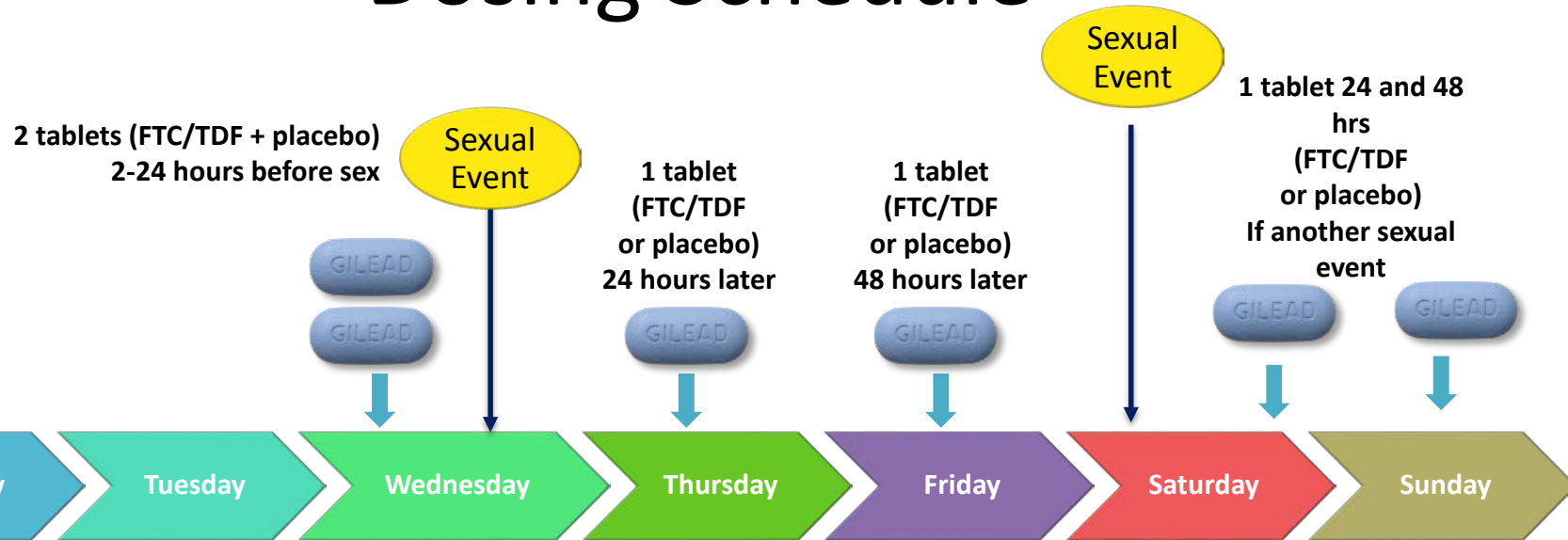
**86%** (95% CI: 40-99,  $p=0.002$ )  
reduction in MSM at high risk of  
HIV infection who took on-demand PrEP



# Dosing Schedule: 1 Sexual Event



# Dosing Schedule



- IPERGAY results provide the first evidence that an event-driven regimen was effective among high-risk MSM with frequent sex
  - Median of 10 sex acts per month and 8 partners every two months.
  - In this study overall, available data suggest that men were taking PrEP an average of three to four days per week
- CDC continues to recommend **daily dosing of PrEP**. Other studies show that daily dosing improves adherence.
- CDC cautions that researchers do not yet know if the Ipergay regimen will work among MSM who have sex less frequently or among other populations at high risk for HIV infection.

# Adherence to PrEP Surrounding Recent Sexual Intercourse

PrEP use, % (min-max)	TVD n=649 sex events	Placebo n=563 sex events
Correct use*	45 (36-57)	40 (22-49)
Suboptimal use	27 (14-35)	31 (18-44)
No PrEP	27 (15-37)	29 (24-44)

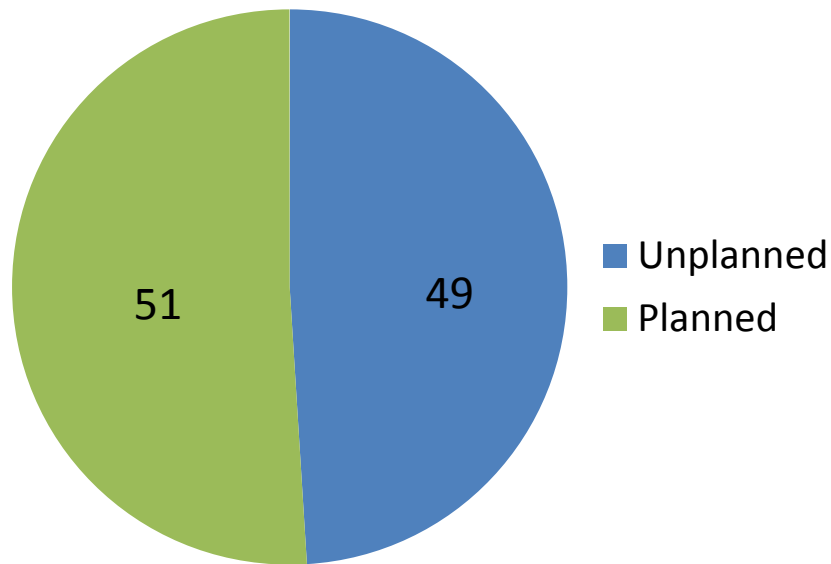
\*According to the protocol or at least one pill before and one pill after sex

**“On demand PrEP” was not used as indicated by the protocol for almost 60% of the 1,212 sexual events reported by the 319 participants**

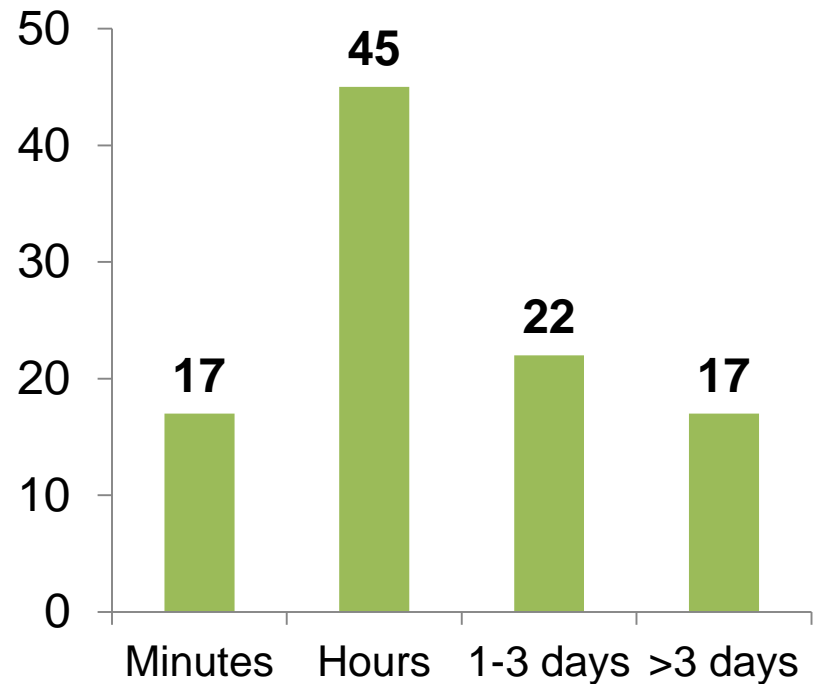
# Planning for the Pre-Event Dose: Social Network Survey

Last anal sex planned

N= 1013 US MSM



How far ahead planned?



**59% reported last sex was unplanned or planned only minutes in advance**



# Purview Paradox: Contradictory Beliefs about Which Providers Will Prescribe PrEP

## **HIV providers:**

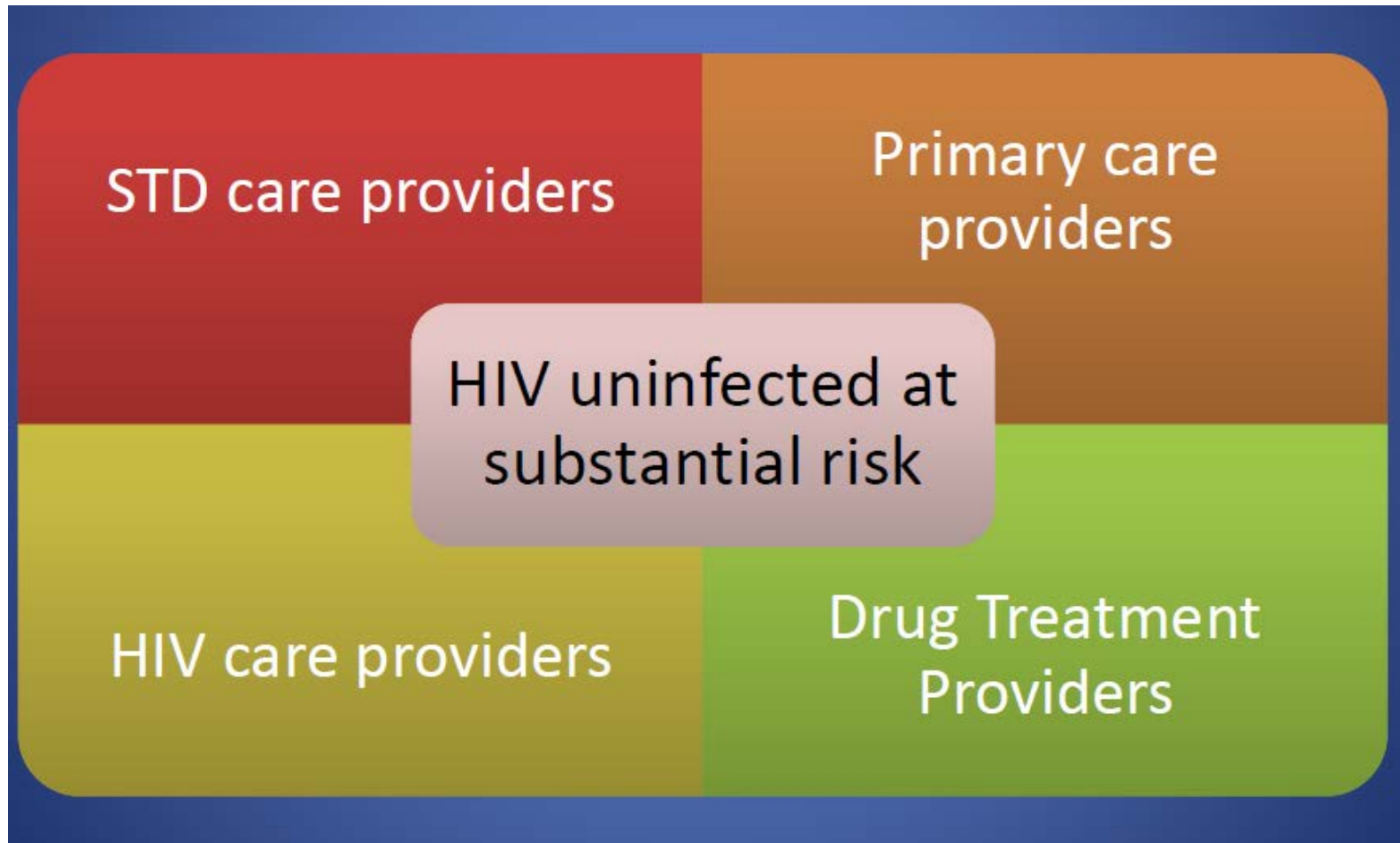
Primary care providers  
are in the best position  
to prescribe PrEP

## **Primary care providers:**

It would not be feasible  
to prescribe PrEP



# Potential PrEP Providers





# HIV Screening Recommendation

- **CDC (2006, revised in 2013)**
  - All patients in all health-care settings
  - High risk patients at least annually
- **USPSTF (2013) GRADE A**
  - Adolescents and Adults 15-65
  - Younger adolescents and older adults at risk

# Assessing for High-Risk Behaviors

Have you ever had a sexually transmitted infection?

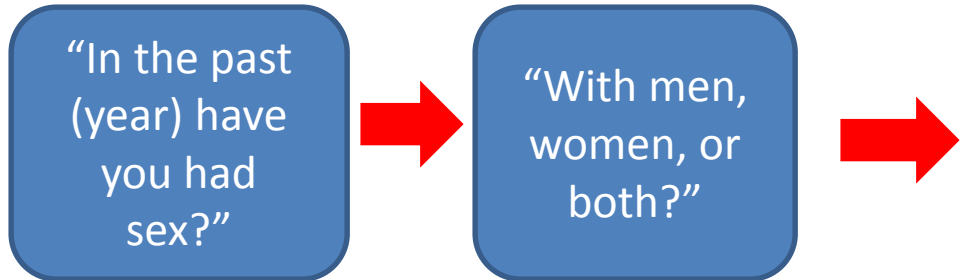
Do you know the HIV status of your partners?

Have you had anal sex? Was it receptive (another person's penis in your anus), insertive (your penis in another person's anus), or both?

Have you exchanged sex for money, goods, or services?

Have you had sex with strangers?

# A tool for risk-stratifying MSM: CDC risk index (“HIRI”)



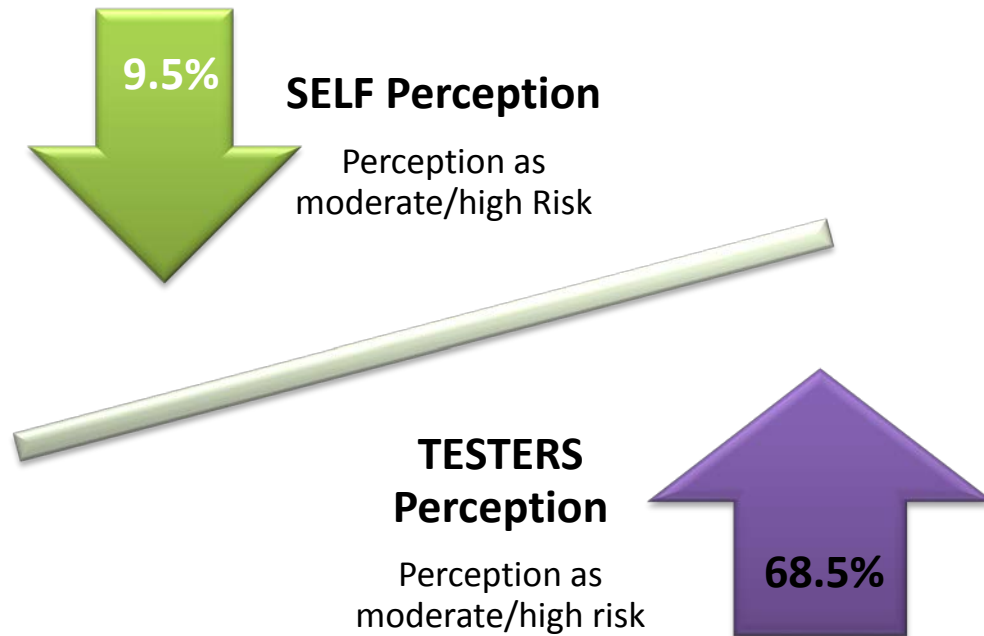
Score < 9: standard prevention  
Score ≥ 10: consider PrEP

HIV-infected in next 6 months?		
Score ≥ 10	Sensitivity 84%	Specificity 45%
	PPV 1.9%	NPV 99.5%

HIRI-MSM Risk Index*			
1	How old are you today (yrs)?	<18 years	score 0
		18–28 years	score 8
		29–40 years	score 5
		41–48 years	score 2
		≥49 years	score 0
2	How many men have you had sex with in the last 6 months?	>10 male partners	score 7
		6–10 male partners	score 4
		0–5 male partners	score 0
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?	1 or more times	score 10
		0 times	score 0
4	How many of your male sex partners were HIV positive?	>1 positive partner	score 8
		1 positive partner	score 4
		<1 positive partner	score 0
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	5 or more times	score 6
		0 times	score 0
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes	score 5
		No	score 0
7	In the last 6 months, have you used poppers (amyl nitrate)?	Yes	score 3
		No	score 0
Add down entries in right column to calculate total score			Total score†

# Self Perception of HIV Risk is Low

Persons (N=3,533; >90% African-American) undergoing HIV rapid testing in Philadelphia were surveyed between July 2012 and Dec 2013



**A large proportion of patients at high-risk for HIV infection do not perceive themselves at high risk**



# CDC Guidance on Prescribing PrEP

- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, screen/treat for STDs, screen/vaccinate for Hep B; pregnancy test) and r/o acute infection
- Prescribe tenofovir-emtricitabine 1 tablet by mouth daily x 90 days
- Provide condoms, adherence and risk-reduction counseling or referral
- Monitor
  - HIV status every 3 months
  - Renal function at 3 months and every 6 months
  - Risk reduction, condoms, STI assessments /rx

US Public Health Service

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

A CLINICAL PRACTICE GUIDELINE



# Medications for prevention- type II diabetes vs sexually-acquired HIV infection

	Metformin	TDF/FTC
Indication (package insert)	indicated as an <u>adjunct to diet and exercise</u> to improve glycemic control...	is indicated <u>in combination with safer sex practices</u> ...reduce the risk of sexually acquired ...
Diagnosis	Impaired fasting glucose (<126 mg/dl) Hemoglobin A1c (5.7-6.4%)	Negative HIV antibody/antigen test Sexual behavior and STI history
Behavioral intervention	Weight loss (at least 7%) Increase physical activity (150 min/wk) Reduce calories and dietary fat intake Education and counseling	Condom use Reduce # of partners Know HIV (tx) status of partners Education and counseling
Clinical assessments/follow-up	Renal function, toxicities (ongoing) A1c every 3-6 months Weight Co-morbidities (e.g., HBP, dyslipidemia)	Renal function, toxicities (ongoing) Hepatitis B infection status HIV every 3 months STI every 6 months
Black box warning	“ <u>Lactic acidosis</u> ... (~0.03 cases/1000 py, ~0.015 fatal cases/1000 py). In more than 20,000 patient-years exposure to metformin in clinical trials, there were no reports of lactic acidosis. “	Lactic Acidosis <0.85/1000 py in HIV+ treatment trials. Not seen in any PrEP trial patients.
Adherence	<b>70%</b> (at least 80% of doses)	<b>77%</b> (4 or more doses/week)



National rapid response for HIV management  
and bloodborne pathogen exposures.



University of California, San Francisco

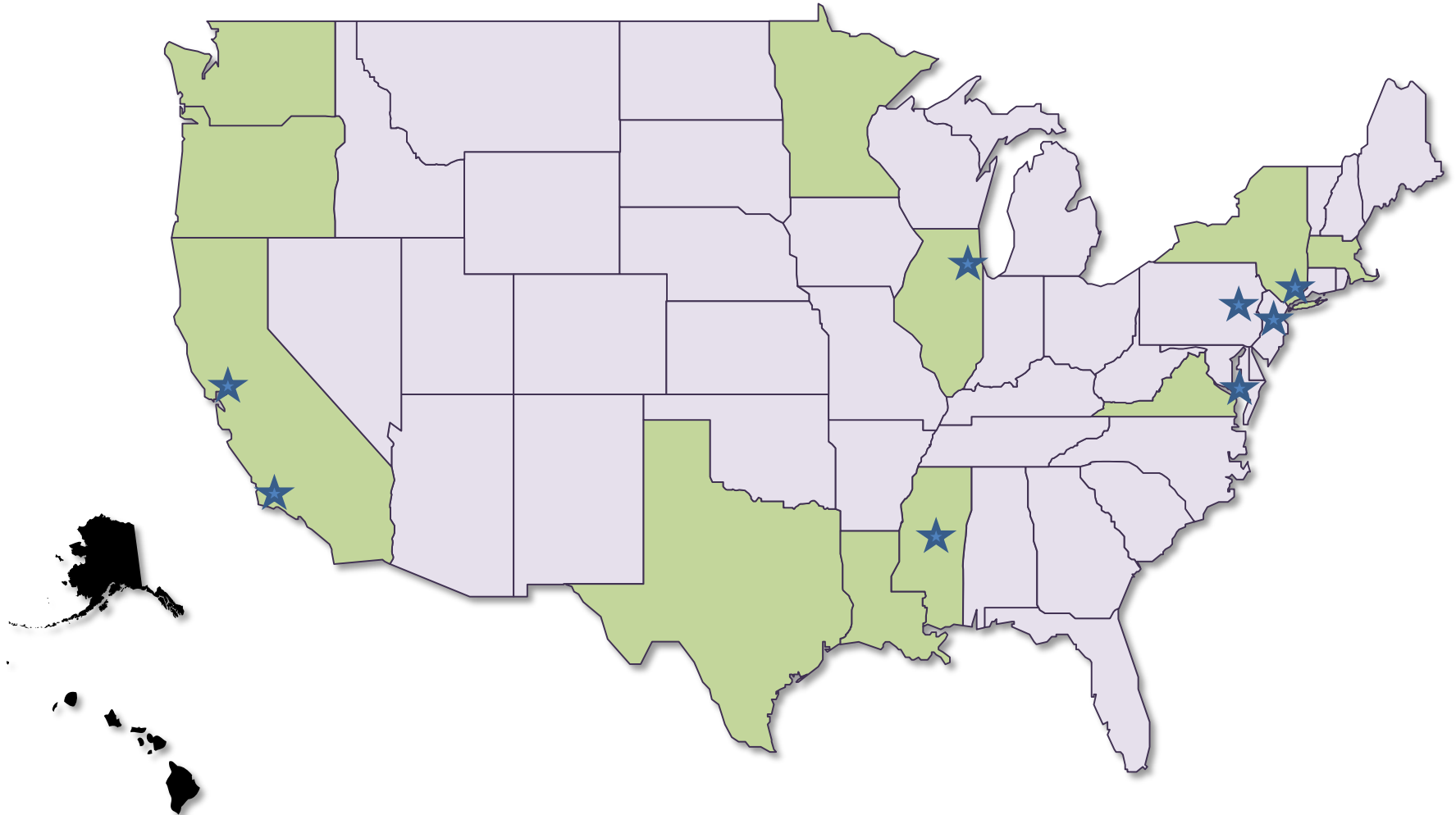
**PrEPline, 855-448-7737**

The CCC Pre-Exposure Prophylaxis  
Service

12 p.m. – 7 p.m. CT

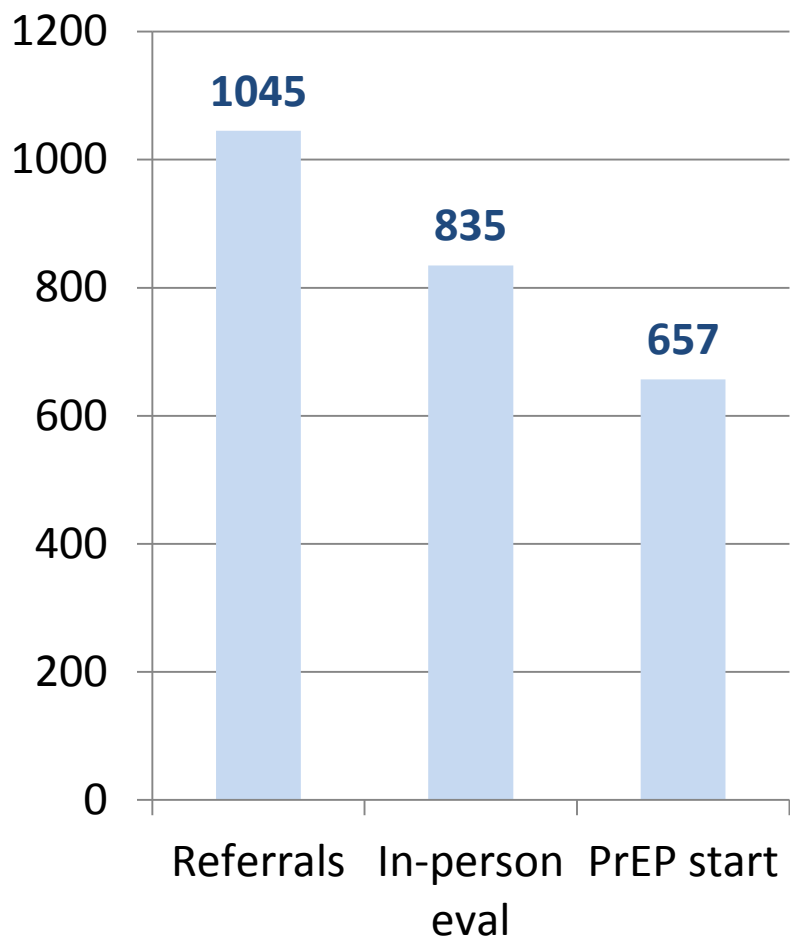
**All other hours: Leandro Mena at 601-815-3885**

# State and County PrEP Initiatives





# PrEP Utilization in a Managed Care System



- 388 person-years of PrEP use
- Mean duration of use 7.2 months
- Mean age 37
- 99% MSM (3 women, 1 trans man)
- Behavioral survey (n=143)
  - Sex partners unchanged in 74%
    - Decrease 15%; Increase 11%
  - Condom use unchanged in 56%
    - Decrease 41%; Increase 3%
- STD: 30% at 6 mo., 50% at 12 mo.
  - No baseline STD data available
- **Zero HIV transmissions**

# 844.YES.PREP

SAY *yes* TO PrEP

Pre-exposure prophylaxis, or **PrEP**, is a way for people who do not have HIV to prevent HIV infection by taking a pill once day. When taken consistently, PrEP has been shown to **reduce the risk of HIV infection in people who are at high risk by up to 92%**.

Post-exposure prophylaxis, or **PEP**, involves taking antiretroviral medicines as soon as possible after you may have been exposed to HIV, to try to reduce the chance of becoming HIV-positive.

**PrEP AND PEP ARE AVAILABLE IN YOUR AREA. CALL TO LEARN MORE.  
844-YES-PREP**

## **WITH OR WITHOUT HEALTH INSURANCE**

Open Arms Healthcare Center (OAHCC)  
500 E Woodrow Wilson Blvd. Suite M  
Jackson, MS 39214

PROJECT BROUGHT  
TO YOU BY



**Assistance is available for both PrEP and PEP for individuals without health insurance or high medical visit or medication co-payment. Call OAHCC at 601-500-7660 for more information.**

**Monday-Friday 7:00 a.m. to 7:00 p.m.**

# Special Populations



Adolescents and Young Adults

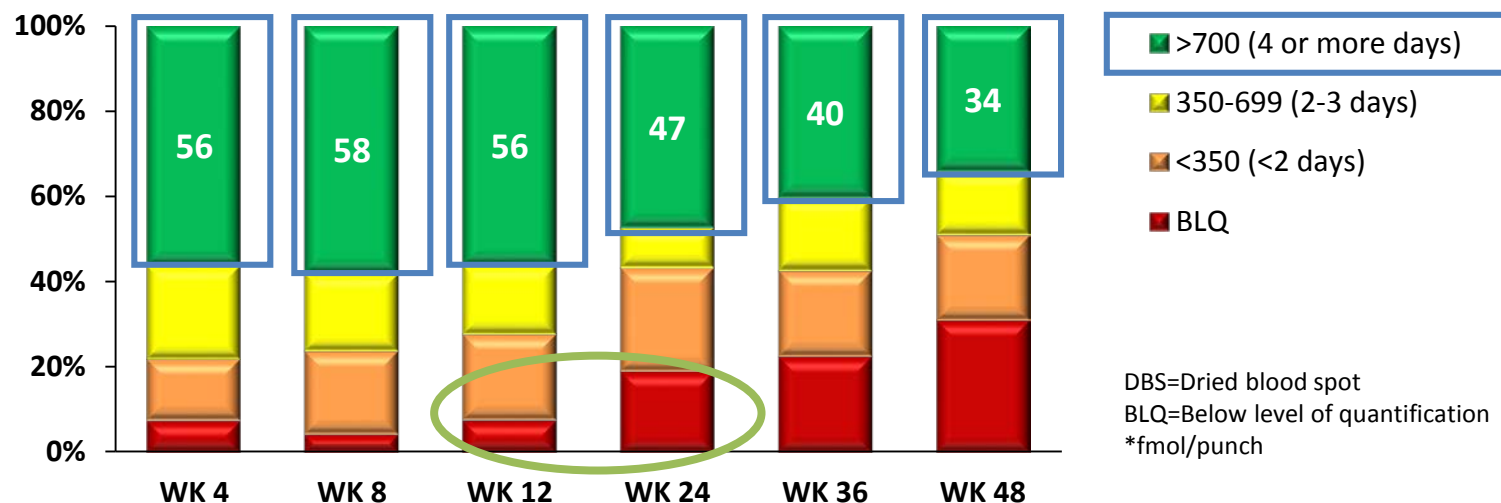


Pregnant and Breastfeeding Women

# PrEP Safety Study of Young Men who Have Sex with Men (YMSM)

Blinded, open-label study among YMSM ages 18-22 years (N=200)

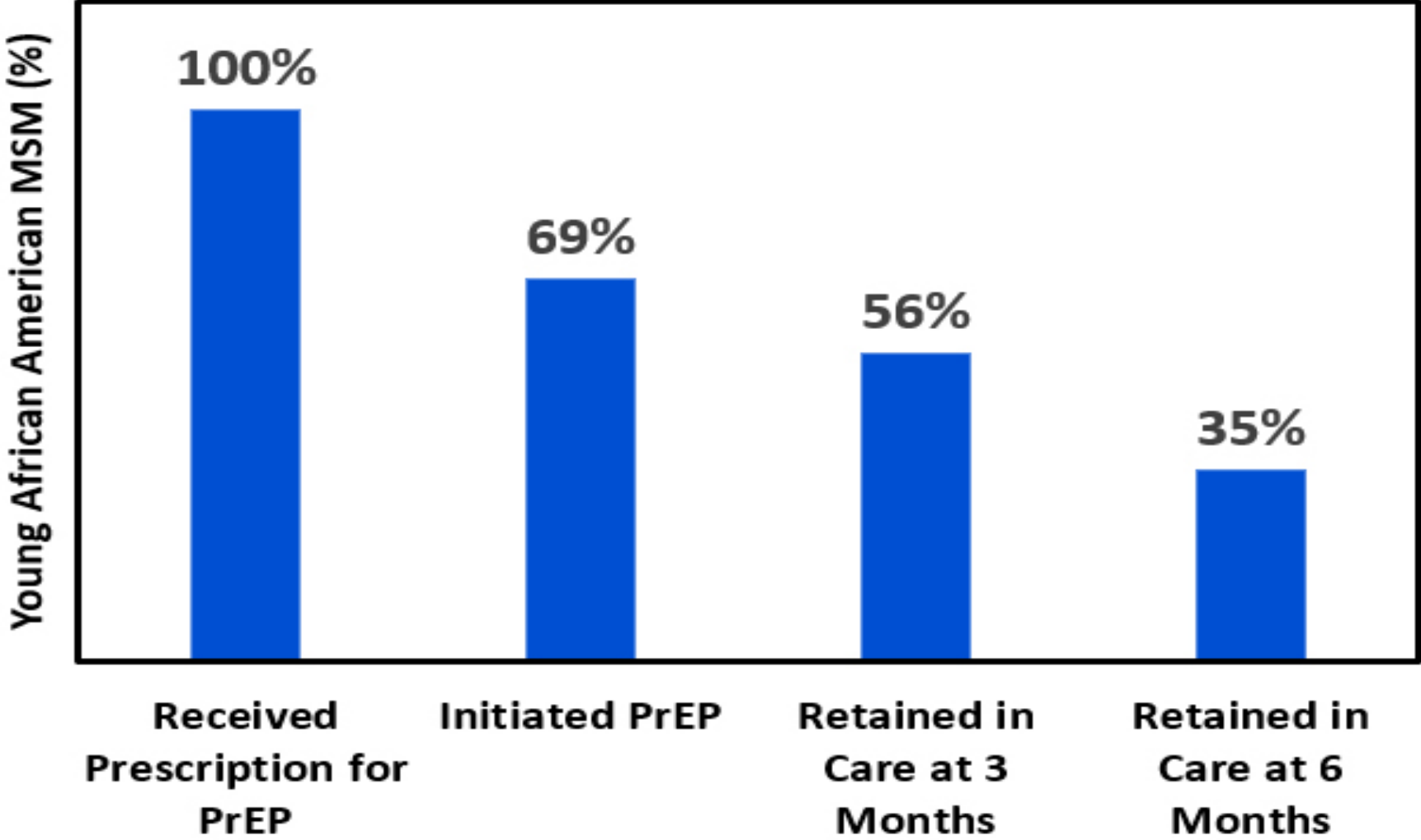
Adherence:  
TFV-DP\* Levels via DBS and Dosing Estimates



**By Week 48, only 34% TVF-DP levels, as measured by DBS, consistent with having  $\geq 4$  doses/week (considered protective level)**

- Adherence decreased for all participants as study visits decreased in frequency at Week 12, regardless of race/ethnicity
- Condomless sex was reported by  $>80\%$  of participants throughout the study
- Condomless anal sex with last partner was associated with higher TFV-DP levels

# AA MSM 18-29 years on PrEP OAHCC



# Pregnancy, Breastfeeding, and PrEP

- Of the men and women with a HIV-negative partner, 46% of men and 51% of women intend to have children<sup>1</sup>
- Oral PrEP may be an option for discordant couples wanting to conceive<sup>2</sup>.
- Combination antiretroviral therapy (cART) for the infected partner may not be fully protective against sexual transmission of HIV.<sup>3</sup>
- Approaches to reduce the risk of HIV transmission during attempted conception for all couples include:<sup>2</sup>
  - Treatment of the HIV-infected partner to achieve maximal viral suppression
  - Truvada for PrEP for the uninfected individual
  - Limiting conception attempts to the periovulation period
  - Screening both partners for STIs and treat for any found
- For HIV+ women with HIV- male partners:<sup>2</sup>
  - Elective male circumcision, artificial insemination, PrEP for male partner
- For HIV+ men with HIV- female partners:<sup>2</sup>
  - Semen collection and processing, continuing PrEP during pregnancy
- Breastfeeding is not recommended with PrEP

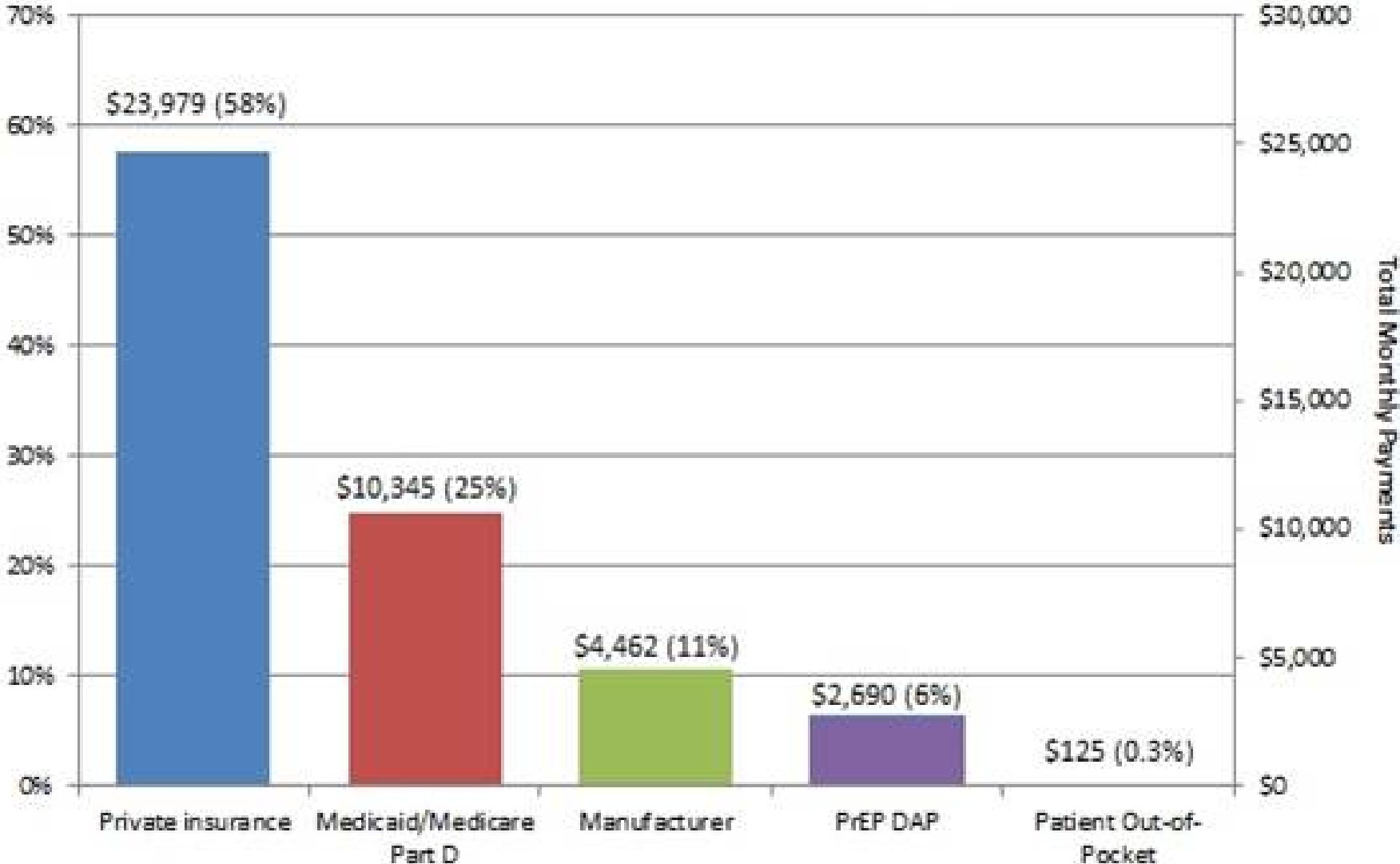
1. Chen JL, et al. Fam Plann Perspect 2001;33:144-52, 165

2. Lampe MA, et al. Am J Obstet Gynecol 2011;204:488.e1-8

3. US Public Health Service Clinical Practice Guidelines. 2014: 1-67. Can be found : <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>

ICD-9	Description	ICD-10	Description
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### Payers for PrEP in an Open-Label Demonstration Study in Seattle, WA



V08	Human immunodeficiency virus infection , asymptomatic	Z21	Asymptomatic human immunodeficiency virus (HIV) infection status
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# Medication Assistance

Gilead will provide Truvada for PrEP at no cost for individuals who qualify for the assistance program

Program Element	Truvada PrEP Medication Assistance Program
Eligibility Criteria	US resident, uninsured or no drug coverage, HIV-negative, low income
Drug Fulfillment	Product dispensed by Covance Specialty Pharmacy, labeled for individual patient use and shipped to prescriber (30 day supply); no card or voucher option
Recertification Period	6 months, with 90 day status check



# How to Access Gilead PrEP Assistance Programs

Alternatively, you can visit [www.start.truvada.com](http://www.start.truvada.com)

## TRUVADA for a Pre-Exposure Prophylaxis (PrEP) Indication

TRUVADA is indicated, in combination with safer sex practices, for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

[Click here for factors that place an uninfected adult at high risk →](#)

[Click here for factors to consider before prescribing TRUVADA for PrEP →](#)

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**Resources for Healthcare Providers** .....

### REMS Resources

Download important Risk Evaluation Mitigation Strategy (REMS) materials for healthcare providers before prescribing TRUVADA for a PrEP indication for uninfected individuals at high risk of sexually acquired HIV-1.

[Read important REMS materials →](#)

### HIV Testing

Read important information about safely prescribing TRUVADA for a PrEP indication, and answer a post-training questionnaire to qualify to offer HIV testing at no cost to uninsured or financially needy individuals.

[Qualify to offer HIV testing at no cost to uninsured or financially needy individuals →](#)

### Medication Assistance Program

Help eligible uninfected individuals taking TRUVADA for a PrEP indication receive assistance paying for the medication.

[Download medication assistance form →](#)

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**View Full Prescribing Information including Boxed Warnings** →

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**View Medication Guide** →

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**For Uninfected Individuals** .....

### Condoms

If you are an uninfected individual at high risk taking TRUVADA for a PrEP indication, you can obtain condoms at no cost.

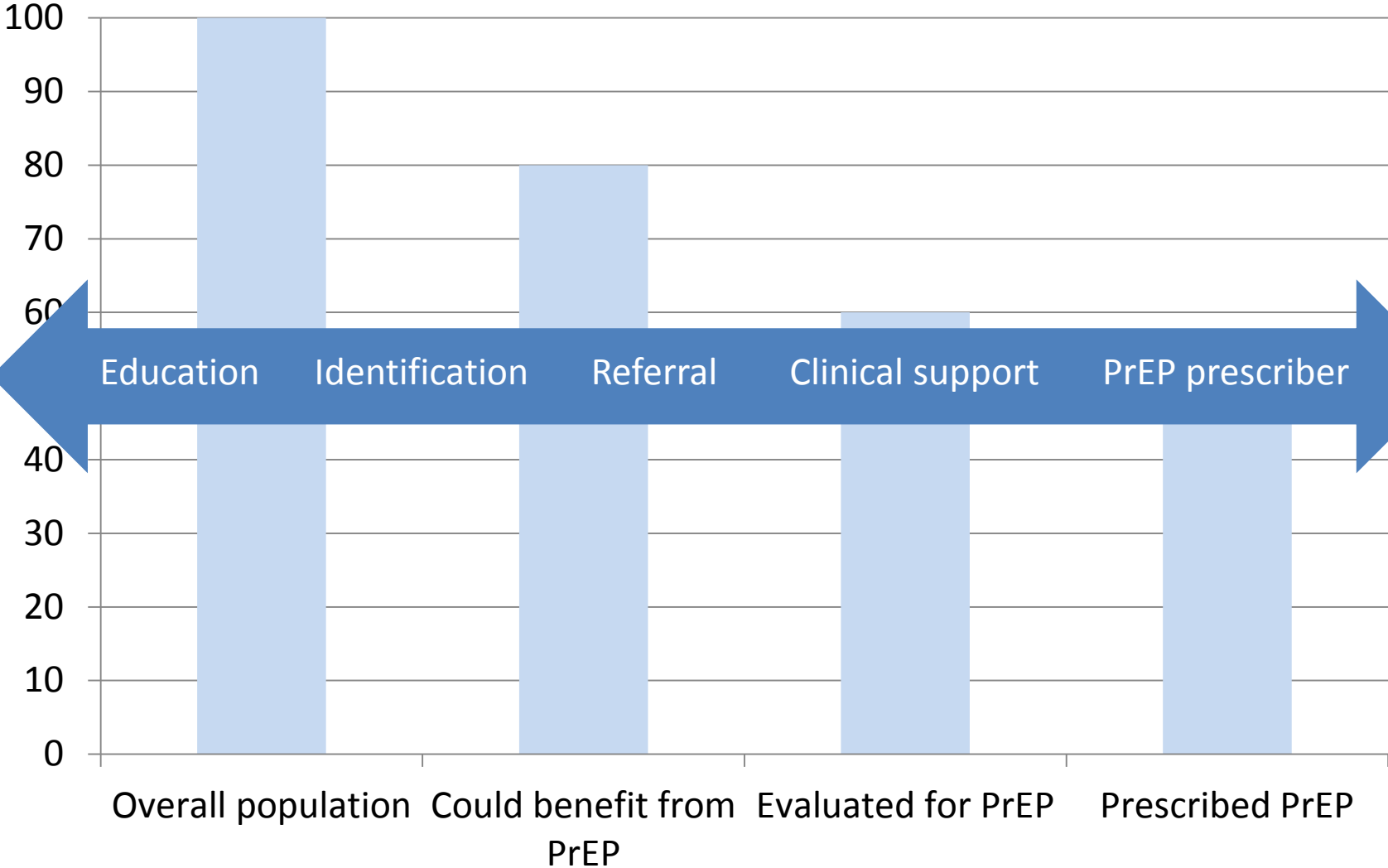
[Open condom ordering form →](#)

### Safety Information for Uninfected Individuals

Review information for uninfected individuals at high risk.

[Review material for uninfected individuals →](#)

# Potential domains of PrEP services



# Open Arms Healthcare Center

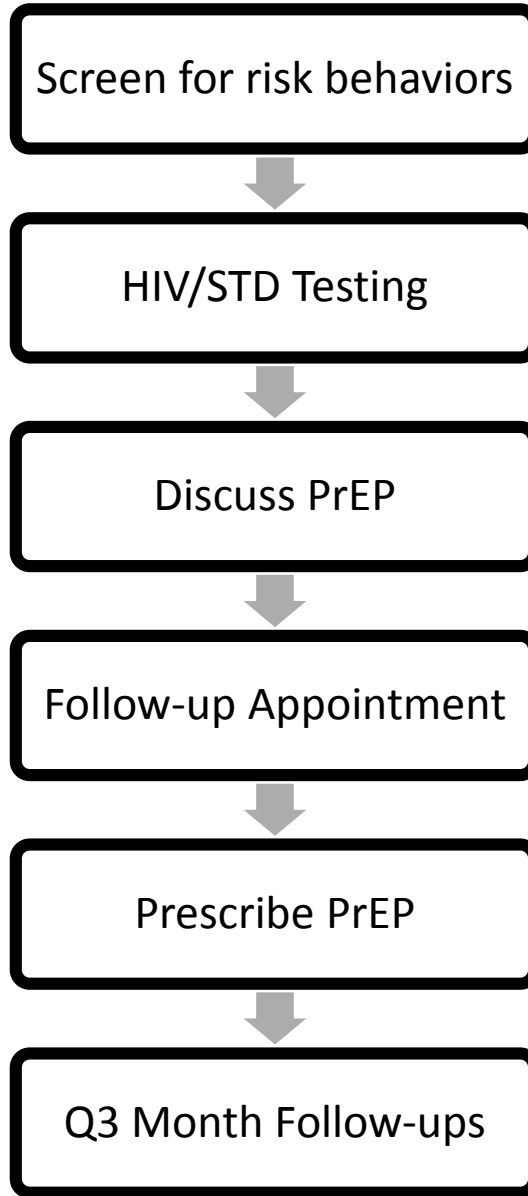


## MSM Tested for HIV 2014 (n=538)

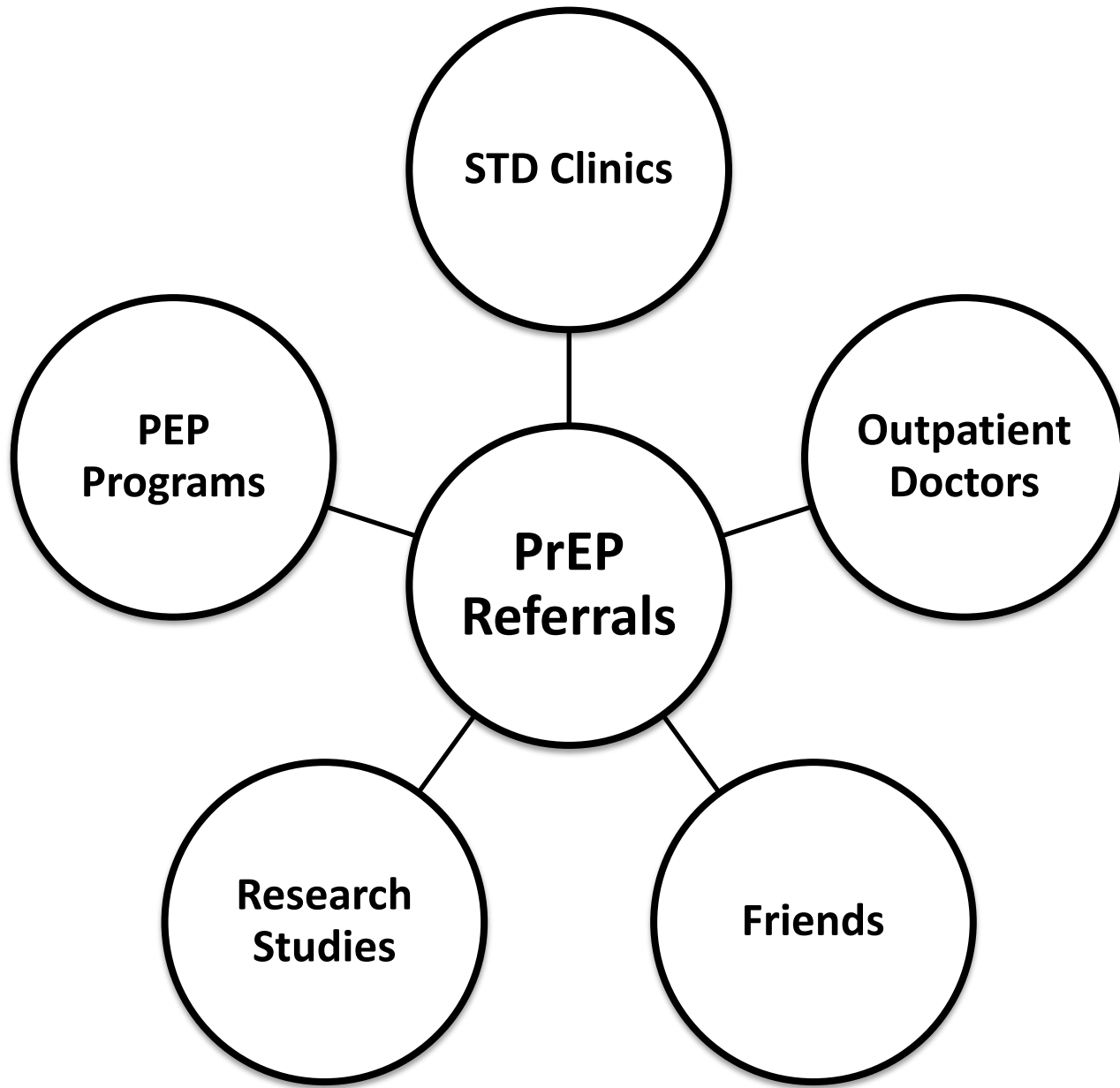
Characteristics	%
Age:	
<18	1
18-24	49
25-34	33
35+	17
Race/Ethnicity:	
White	11.1
African-American	78.3
Other	<1
Hispanic	7.2
HIV-positive rate	12.9

- Located in Jackson, MS
- Opened in 2012
- LGBT Healthcare
- Staff: 2 MDs (PT), 1 NP, 1 Clinical Psychologist, 1 RN, 1 LPN, 1 NA, 2 Case Managers
- PrEP awareness
  - 2014: < 15%
  - 2015: 28%

# Open Arms Healthcare Center



**PrEP IMPLEMENTATION**



# Patients' Experiences



- “Peace of mind”
- Challenges to adherence
  - Storage and incorporation in daily routine
- Experiences with frequent testing
  - Positive reflections on routine testing and clinic visits
  - “I want to be healthy”

# Future of PrEP

- PrEP of 2015 will not necessarily be the PrEP of 2020 or 2030
- Ongoing research needed on women, adolescents, youth (15-17 currently being studied in ATN 113)
- Potential novel agents for PrEP and/or novel delivery systems:
  - Tenofovir alafenamide for PrEP (pro-drug to TDF) less buildup in bones and kidneys
  - IM long acting integrase inhibitor- will be studied in HPTN
  - Tenofovir vaginal ring (pending phase 1 data)
  - Long-acting tenofovir alafenamide (GS-7340) subdermal implant
- Additional ongoing research on different dosing regimens:
  - HPTN 067
  - IPERGAY open label

# National HIV/AIDS Strategy

- **Goal 1:** Reducing new HIV infections
- **Goal 2:** Increasing access to care and improving health outcomes for people living with HIV
- **Goal 3:** Reducing HIV-related disparities and health inequities
- **Goal 4:** Achieving a more coordinated national response to the HIV epidemic

## NATIONAL HIV/AIDS STRATEGY for the UNITED STATES:

UPDATED TO 2020

JULY 2015





# Resources, Web/Video

- **UMMC AIDS Education and Training Center**
  - Technical Assistance
- Ken Like Barbie: The Frontier of HIV Prevention is Changing - A Video Fact Sheet on PrEP
  - <http://myprepexperience.blogspot.com/2013/05/ken-like-barbie-frontier-of-hiv.html>
- Project inform: videos, booklets
  - <http://www.projectinform.org/prep/>
- YouTube
  - <https://www.youtube.com/watch?v=aVvhMsFRa-M&feature=youtu.be>
  - <http://men.prepfacts.org>
  - [https://www.youtube.com/watch?v=RXtRfNEMiuE&index=17&list=PLhAEglxleeK\\_ZmjwiZW0XKnImKJU5o66E](https://www.youtube.com/watch?v=RXtRfNEMiuE&index=17&list=PLhAEglxleeK_ZmjwiZW0XKnImKJU5o66E)
  - [https://www.youtube.com/watch?v=KoMFKoup2kA&index=18&list=PLhAEglxleeK\\_ZmjwiZW0XKnImKJU5o66E](https://www.youtube.com/watch?v=KoMFKoup2kA&index=18&list=PLhAEglxleeK_ZmjwiZW0XKnImKJU5o66E)
  - <https://www.youtube.com/watch?v=-Xx92whZS0o>
- Fenway
  - <http://thefenwayinstitute.org/prepinfo/>

