

PrE-Exposure Prophylaxis (PrEP) A Tool at Your Hand to Fight HIV



Proven. Effectiveness. PrEP.

Laura Beauchamps, MD
Assistant Professor
Division of Infectious Diseases
University of Mississippi Medical Center
Principal Investigator Mississippi AETC

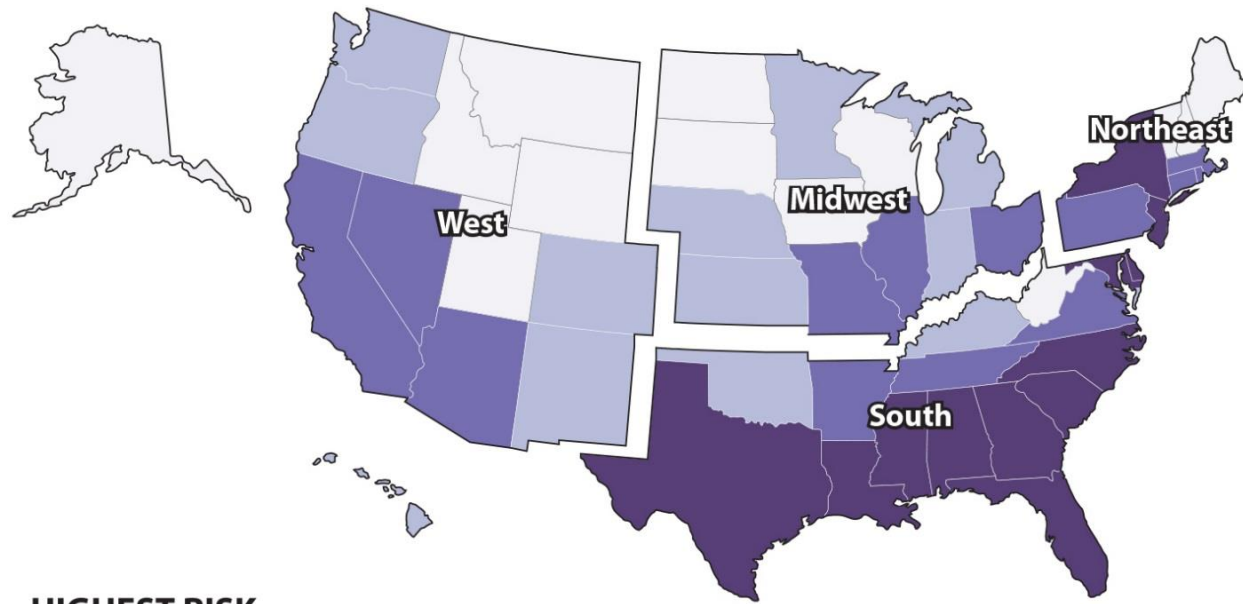
Disclosures

- I have no relevant financial disclosures

Objectives

1. To understand the rationale for PrEP
2. To review PrEP efficacy data
3. Summarize CDC Guidelines on HIV PrEP
4. Review some case scenarios of PrEP candidates and strategies
5. Review documentation and billing approaches for various patient populations
6. Review future directions for PrEP

Lifetime Risk of HIV Diagnosis by State



HIGHEST RISK

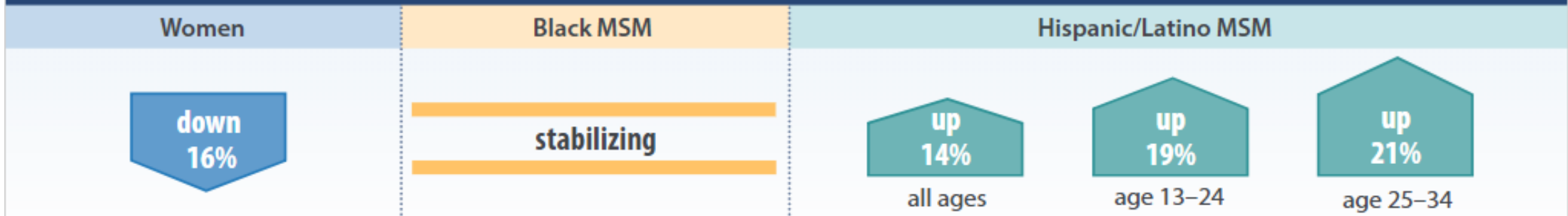
LOWEST RISK

State	One in "n"	State	One in "n"	State	One in "n"	State	One in "n"
District of Columbia	13	Nevada	98	Michigan	167	West Virginia	302
Maryland	49	Illinois	101	Oklahoma	168	Wisconsin	307
Georgia	51	California	102	Kentucky	173	Iowa	342
Florida	54	Tennessee	103	Indiana	183	Utah	366
Louisiana	56	Pennsylvania	115	Washington	185	Maine	373
New York	69	Virginia	115	Colorado	191	Alaska	384
Texas	81	Massachusetts	121	New Mexico	196	South Dakota	402
New Jersey	84	Arizona	138	Hawaii	202	New Hampshire	411
Mississippi	85	Connecticut	139	Oregon	214	Wyoming	481
South Carolina	86	Rhode Island	143	Minnesota	216	Vermont	527
North Carolina	93	Ohio	150	Kansas	262	Idaho	547
Delaware	96	Missouri	155	Nebraska	264	Montana	578
Alabama	97	Arkansas	159			North Dakota	670

Source: Centers for Disease Control and Prevention

39,782 • Total HIV Diagnoses in 2016

HIV Diagnoses Trends from 2011–2015



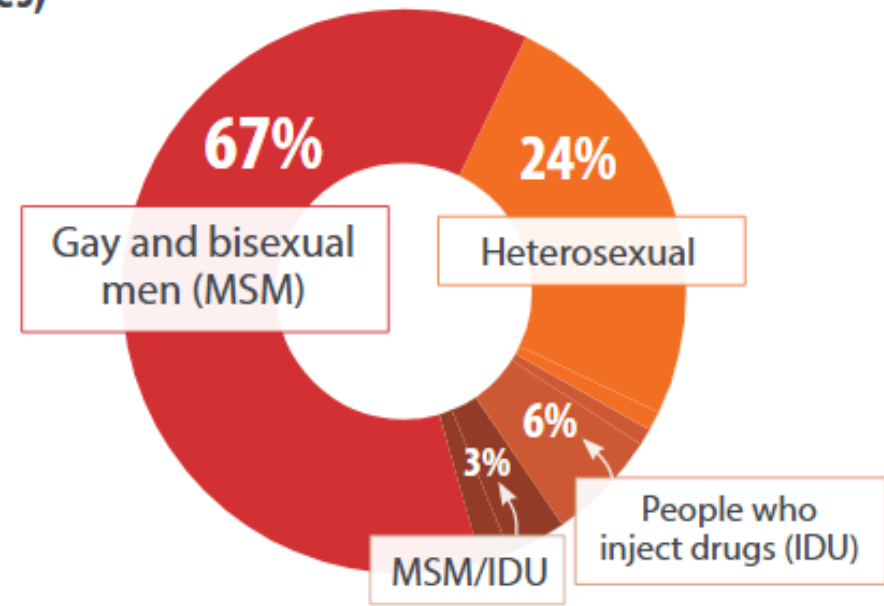
Percentage HIV Diagnoses in 2016

Blacks/African Americans accounted for **44%** of HIV diagnoses, though they comprise only **12%** of the US population



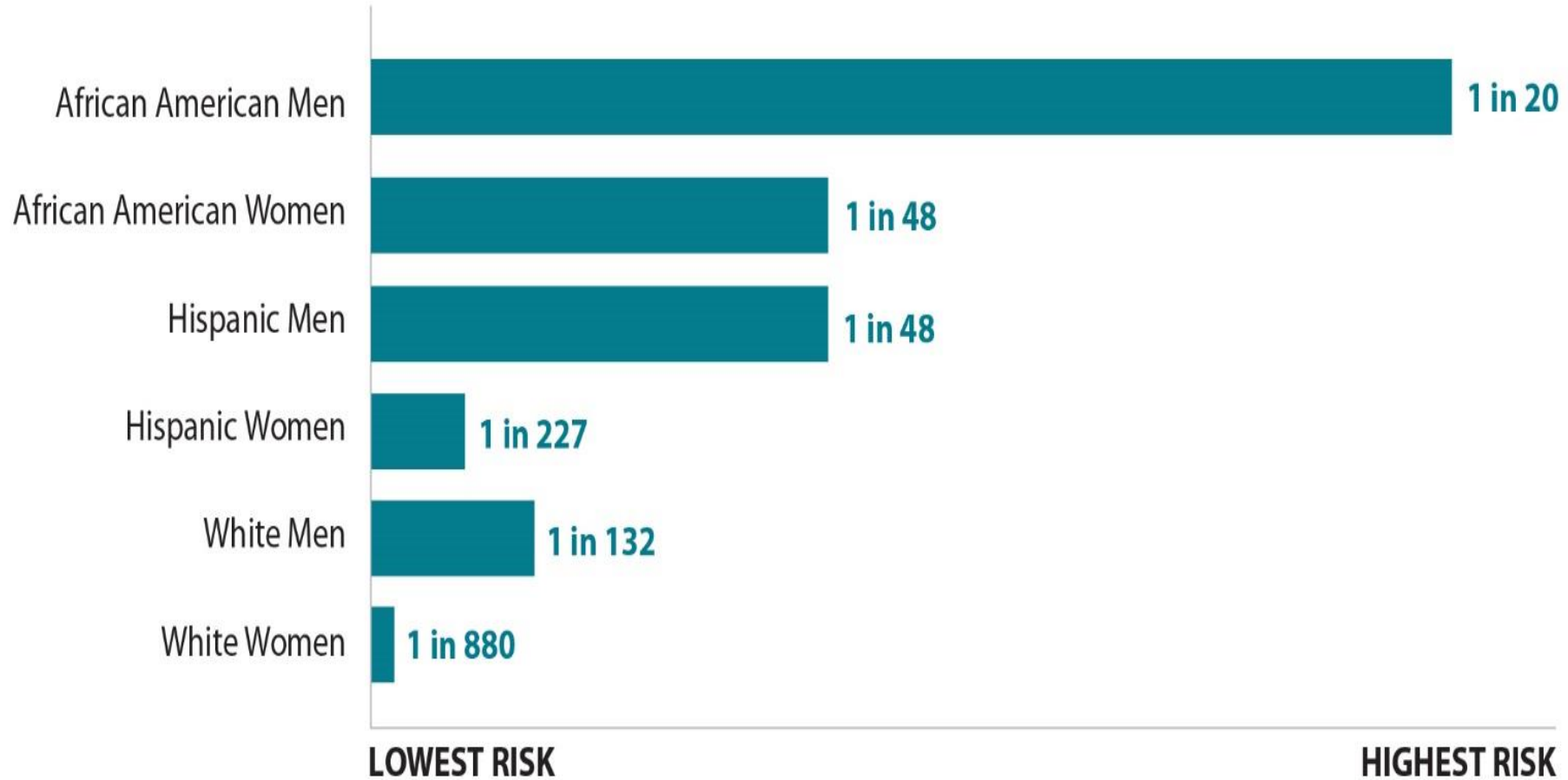
■ black/African American
 ■ White
 ■ Hispanic/Latino
 ■ Other*

*American Indian/Alaska Native: 0.6% • Asian: 2.5% • Native Hawaiian/Other Pacific Islander: 0.1% • Multiple races: 2.2%



Source: Centers for Disease Control and Prevention

Lifetime Risk of HIV Diagnosis by Race/Ethnicity



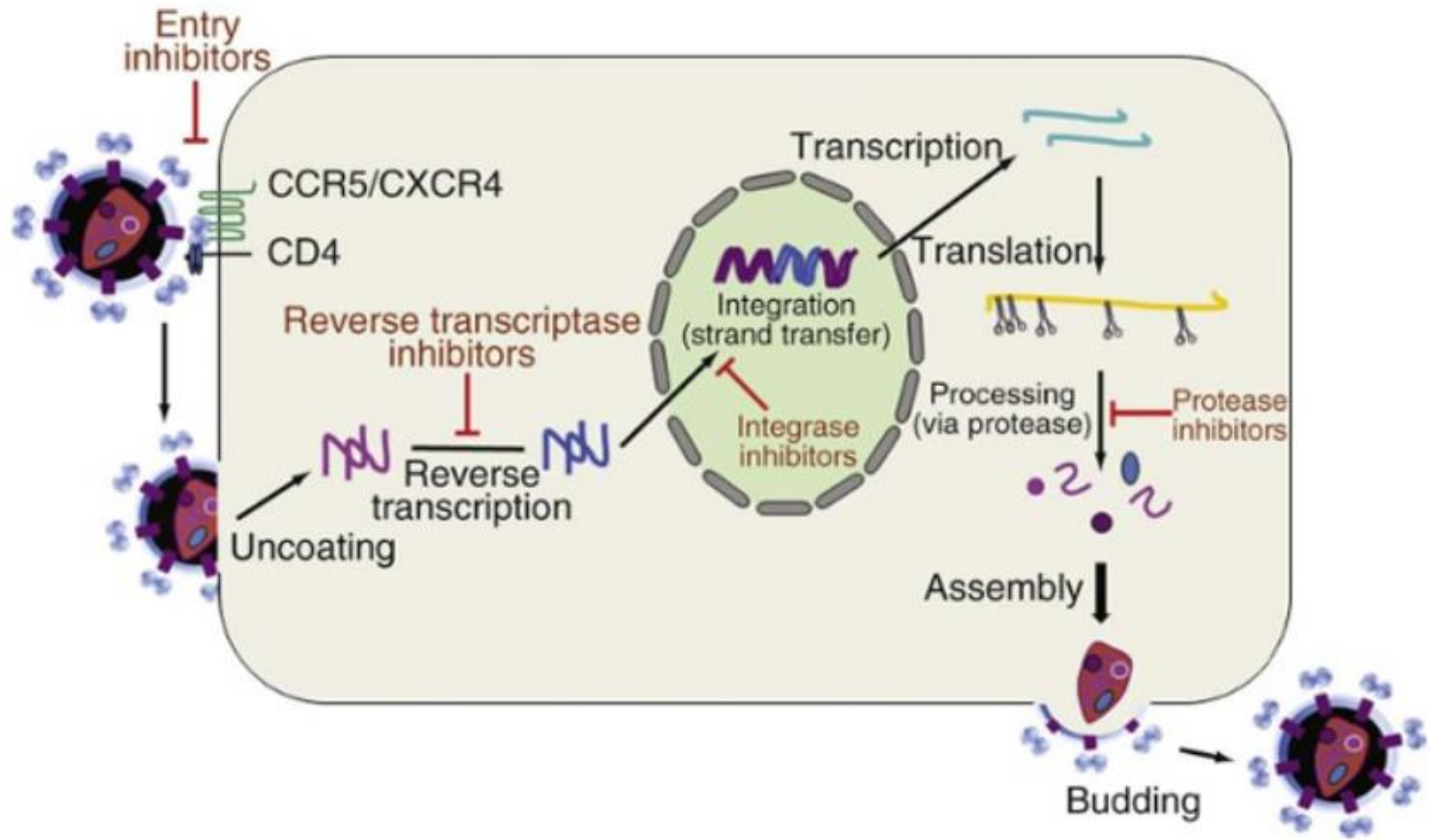
Source: Centers for Disease Control and Prevention

Context

- By the time I finish talking today, 5 new people in the United States will have contracted HIV
- In Jackson, if you are a black man who has sex with men (MSM), your lifetime risk of contracting HIV is 1 in 2
- Among metropolitan areas in the United States, Jackson ranks #4 for new HIV diagnoses

So how does PrEP work?

- Rationale: Having HIV drugs present at the site of exposure should reduce the risk of infection
- Recommended for high-risk individuals by the CDC and World Health Organization (WHO)
- There is currently one FDA approved medication for HIV PrEP



Drugs used to treat HIV

- **Protease Inhibitors (PI)**

- Saquinavir (Invirase)
- Fosamprenavir (Telzir)
- Darunavir (Prezista)
- Ritonavir (Norvir)
- Atazanavir (Reyataz)
- Nelfinavir (Viracept)
- Indinavir (Crixivan)
- Tipranavir (Tipranavir)

- **Integrase Strand Transfer Inhibitors (Insti)**

- Raltegravir
- Elvitegravir
- Dolutegravir (Tivicay)
- Bictegravir

- **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**

- Nevirapine
- Rilpiverine (Eduvant)
- Delavirdine
- Efavirenz (Sustiva)
- Etravirine (Intelence)

- **Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**

- Zidovudine (Retrovir)
- Abacavir (Ziagen)
- Didanosine (Videx)
- Tenofovir (Viread)
- Stavudine (Zerit)
- Emtricitabine (Emtriva)
- Lamivudine (Epivir)

- **Entry Inhibitors**

- Enfuvirtide (Fuzeon)
- Maraviroc (Selzentry)

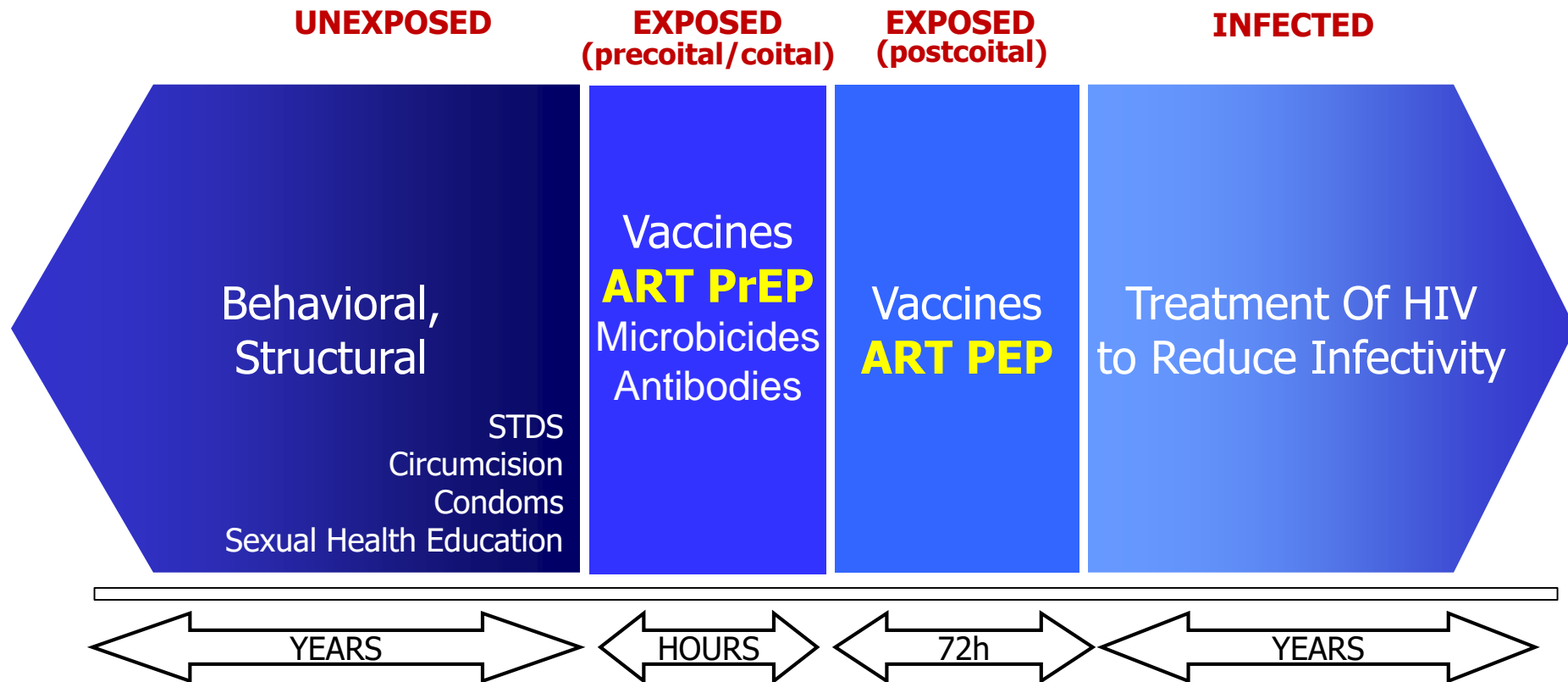


PrEP Medication

- Tenofovir disoproxil fumarate – Emtricitabine (TDF-FTC) was FDA approved in 2012 for HIV PrEP
- TDF-FTC is used in many daily regimens among HIV-positive patients in combination with either an integrase inhibitor (INSTI) or a protease inhibitor (PI)
- Currently, it is the first (and only) medication approved for PrEP by the FDA

Timing of Prevention Opportunities

Cohen et al., JCI, 2008
Cohen et al., JIAS, 2008



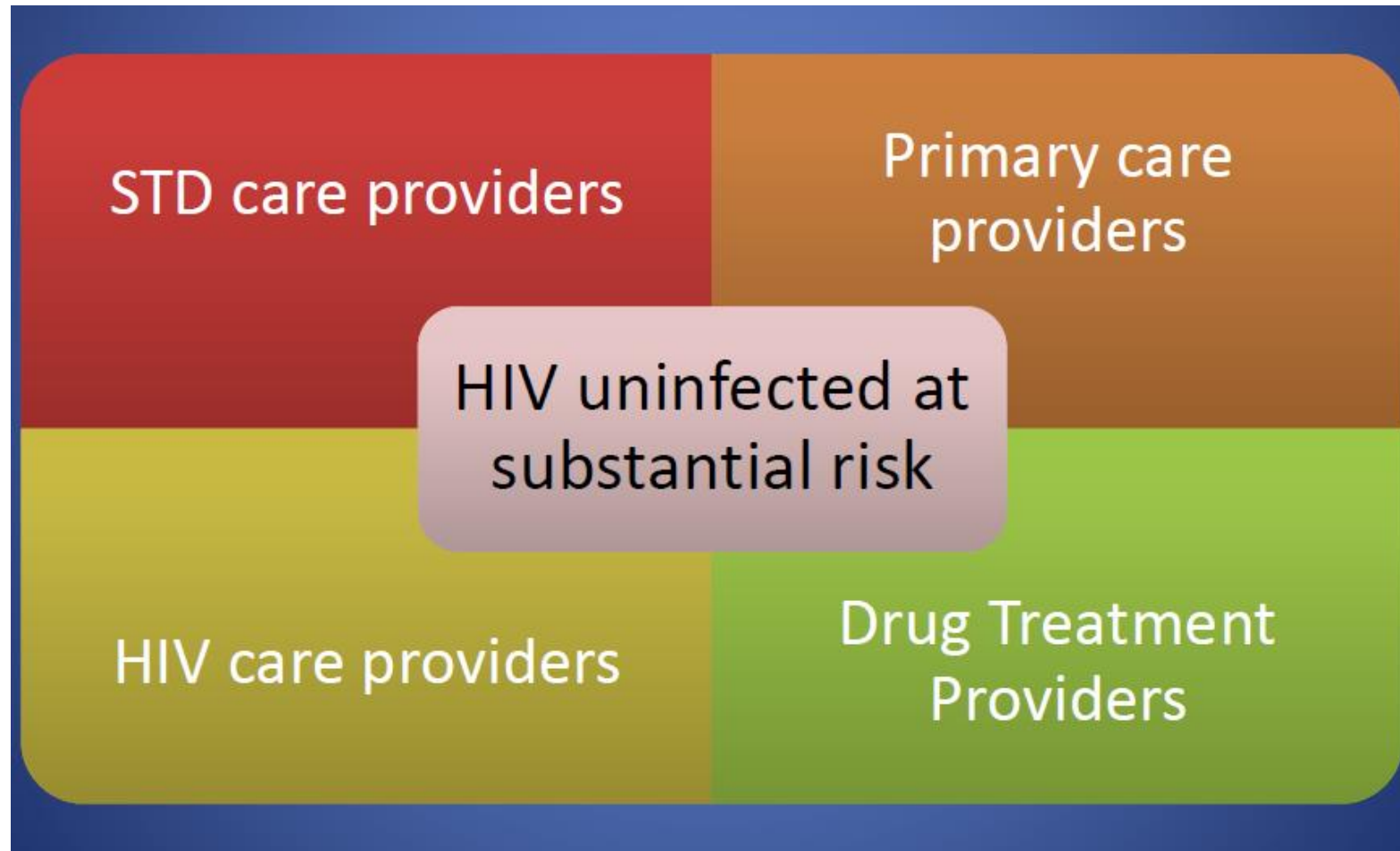
PrEP: Results from Clinical Trials

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

- 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

US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014.
<http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>.

Potential PrEP Providers



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



Labs to order in every PrEP visit

- HIV antibody/antigen LAB 5933
- RPR LAB 494
- C. trachomatis/N. gonorrhoeae PCR, Urine LAB 1376 (urine pipetted into yellow Cobas tube)
- N. gono PCR, throat LAB 5899 (Aptima swab and medium, physician/nurse collected)
- N. gono PCR, rectal LAB 5899 (Aptima swab and medium, patient collected)
- C. trach PCR, throat LAB 5903 (Aptima swab and medium, physician/nurse collected)
- C. trach PCR, rectal LAB 5903 (Aptima swab and medium, patient collected)
- Creatinine or BMP
- Urinalysis after initiation and annually

Financing of PrEP: Billing

A 25 yo male presents concerned about condomless anal sex with another man and request an HIV test. MD notices that the patient is also due for a well visit this visit and performs it. MD Decides to perform a preventive medicine visit exam, spends 35 min counseling including PrEP and performs a rapid HIV test as well as screening for syphilis, CT/GC including extra-genital sites, and orders a serum creatinine. Patient has been vaccinated for HBV.

Service	ICD-10 Code
General Medical Exam (WV)	Z0000
Special screening for other specified viral disease (HIV screening)	Z1159
HIV Counseling	Z717
High Risk Sexual Behavior	Z7251

Financing of PrEP: CPT codes for prevention counseling

CPT	Description
99401	Prevention Counseling (15 minutes)
99402	Prevention Counseling (30 minutes)
99403	Prevention Counseling (45 minutes)
99404	Prevention Counseling (60 minutes)

Financing of PrEP: Billing Codes

ICD-10*	Description
Z72.5	High risk sexual behavior
Z20.82	Contact with and (suspected) exposure to other viral communicable diseases
Z20	Contact with and (suspected) exposure to communicable diseases
Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
Z20.6	Contact with and (suspected) exposure to HIV
Z77.21	Contact with and (suspected) exposure to potentially hazardous body fluids
W46	Contact with hypodermic needle: "the appropriate 7th character is to be added to each from category W46" A-initial encounter, D-subsequent encounter, S-sequela
W46.0	Contact with hypodermic needle (hypodermic needle stick NOS)
W46.1	Contact with contaminated hypodermic needle

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

PrEP Assistance Program

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 →](#)

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 →](#)

[View Full Prescribing Information including Boxed Warnings →](#)

[View Medication Guide →](#)

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 →](#)



Family Planning Waiver

Eligibility Criteria:

- Family income is at or below 194% of the federal poverty level (FPL)
- Must be capable of reproducing ages 13-44 years of age.
- Must not have had a procedure that prevents them from reproducing.
- Must not have Medicare, CHIP, or any other health insurance or third party medical coverage

Benefits:

- Family planning and related services
- One annual visit and up to three subsequent visit (not to exceed four visits per federal fiscal year.
- Effective January 1, 2015, beneficiaries enrolled in the Family Planning waiver demonstration program may have a prescription for contraceptives and/or medications to treat a sexually transmitted infection (STI)/sexually transmitted disease (STD) written by any Medicaid participating provider filled at their local Medicaid participating pharmacy.

Assistance for Insured Patients

1

Gilead Advancing Access Co-pay Card

gileadcopay.com
877-505-6986

- \$3,600 max/calendar year
- No income restrictions
- Covers co-pays, deductibles and co-insurance
- 12-month enrollment, reapply
- Proof of US residence (utility bill, etc.)
- Not used with state/federal plans, such as Medicare (apply to PAF or PAN Foundation).

If the pharmacy doesn't accept Gilead's Co-pay Card, keep sales and pharmacy receipts. Call the number on the back of co-pay card. Submit paperwork for reimbursement for every refill.

2

Patient Advocate Foundation (PAF)

<https://www.copays.org/diseases/hiv-aids-and-prevention>

- \$5,000 max/year, re-apply
- Income <400% FPL (\$47,080)
- Based on taxable income (1040 line 7, 1040 EZ line 1)
- Must be insured (as listed under "YES" above)
- Covers co-pays only
- Proof of US residence (utility bill, etc.)
- Case managers available to help resolve medical cost issues (800-532-5274)

3

Patient Access Network Foundation

panfoundation.org/hiv-treatment-and-prevention
866-316-7263

- \$4,000 max/year, re-apply
- Income <500% FPL (\$58,850)
- Based on taxable income (1040 line 7, 1040 EZ line 1)
- Must be insured (as listed under "YES" above)
- Covers co-pays, deductibles and co-insurance
- Proof of US residence (utility bill, etc.)
- Pharmacies can bill PAN Foundation directly

Open Arms Healthcare Center

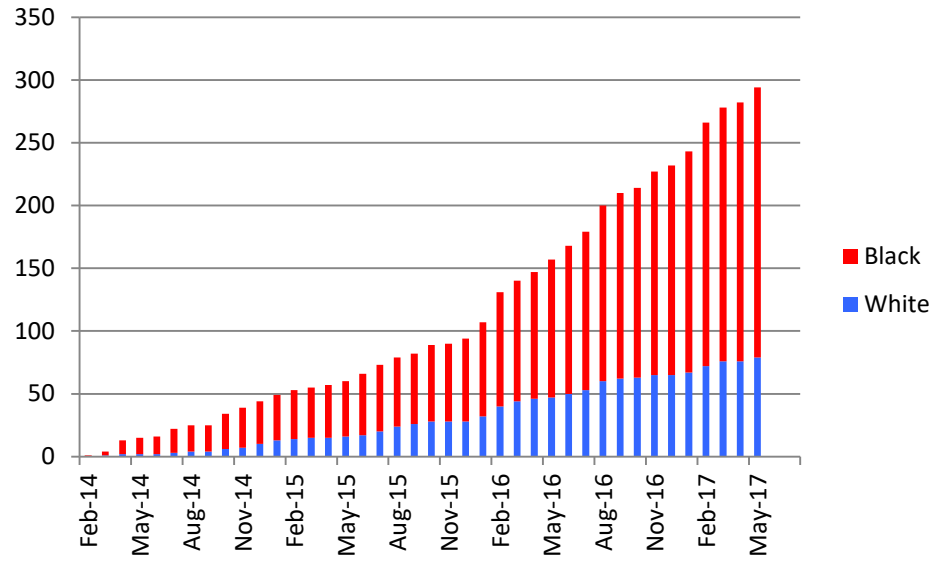
- Located in Jackson, MS
- Opened in 2013
- LGBT friendly Healthcare
- Staff: 4 MDs , 1 NP, 1 Clinical Psychologist, 2RN, 2 LPN, 1 PN, 3 Case Managers
- PrEP awareness
 - 2014: < 15%
 - 2015: 28%



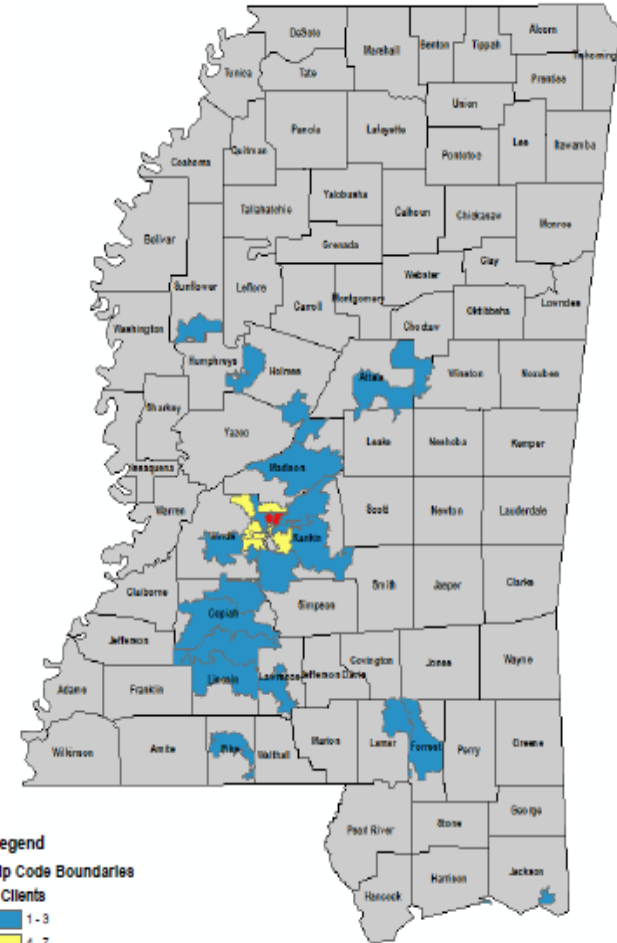
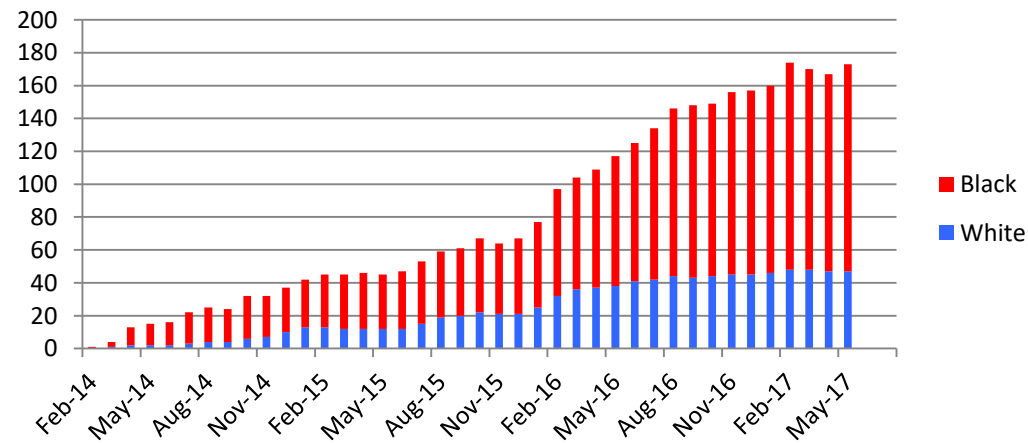
MSM Tested for HIV 2014 (n=538)

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

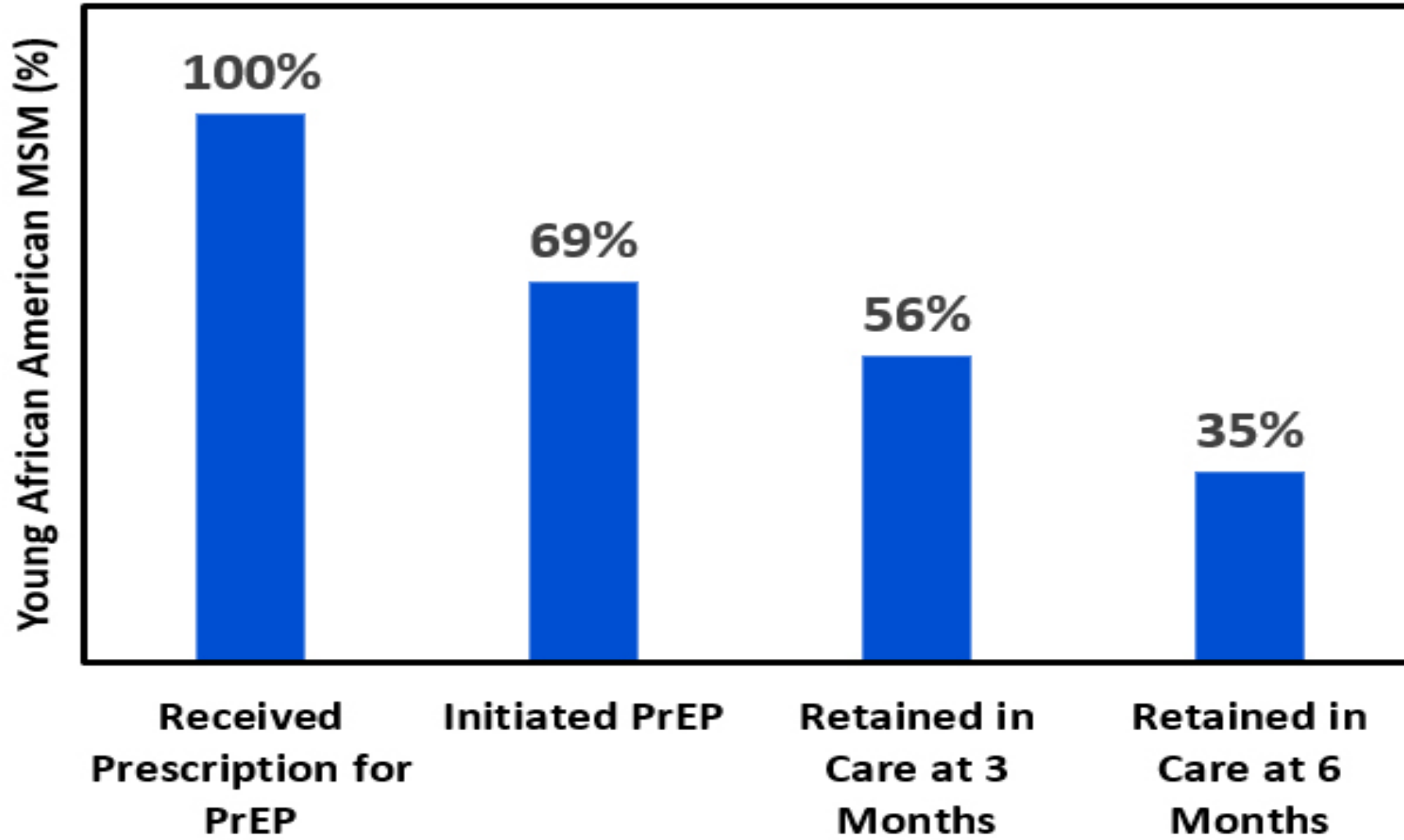
Total Initiated on PrEP



Total Patients on PrEP



AA MSM 18-29 years on PrEP OAHCC



Case 1

- A 24 year old man is presenting to you for primary care establishment. He is currently sexually active with men, and has been active with multiple men within the last 3 months. He engages in oral and anal sex with inconsistent condom use. He has no medical history and no previous STI history.
- Vitals and physical examination are unremarkable.
- His pre-visit labs performed a week ago were negative for HIV and other STIs

Case 1

- Is this patient a candidate for PrEP?
- A. Yes, start now
- B. Not a candidate

Case 1

- According to the CDC, MSM who fulfill the following criteria are candidates:
 - Adult man
 - Without acute or established HIV infection
 - Any male sex partners in the past 6 months
 - Not in a monogamous partnership with a recently tested, HIV negative man

AND at least one of the following:

- Any anal sex without condoms (receptive or insertive) in past 6 months
- Any STI diagnosed or reported in past 6 months
- Is in an ongoing relationship with an HIV-positive male partner

Who is “high risk?”

MSM

Condomless anal sex

Recent sexually-transmitted infection

HIV-infected partner

Heterosexual adults

Condomless sex with a partner who injects drugs or is a bisexual man

HIV-infected partner

Injection drug users

Use of shared injection equipment

Case 1

- Which tests must be sent before starting PrEP?
 - A. HIV antibody, Hepatitis B surface antibody, urinalysis
 - B. HIV antibody, Hepatitis B surface antigen, serum creatinine
 - C. HIV RNA, hepatitis B surface antibody, urinalysis
 - D. HIV RNA, hepatitis B surface antigen, serum creatinine

Case 1

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 - A. HIV antibody, Hepatitis B surface antibody, urinalysis
 - B. HIV antibody, Hepatitis B surface antigen, serum creatinine**
 - C. HIV RNA, hepatitis B surface antibody, urinalysis
 - D. HIV RNA, hepatitis B surface antigen, serum creatinine

What side effects should you counsel the patient on?

- Nausea may occur with initiation of TDF-FTC; it typically resolves over time
- Kidney injury rarely occurs (~2% in iPrex)
 - Periodic monitoring is obligatory and abnormalities usually resolve with drug discontinuation
- A small decrease in bone mineral density may occur; however this does not appear to be clinically significant at this time
- Antiretroviral resistance is unlikely but possible

How would you counsel him about...

- The length of time on PrEP before he is maximally protected?
 - About 7 days, when maximal levels are achieved in rectal tissue
- If stopping PrEP, how long should he take it beyond his last high-risk sexual encounter?
 - 4 weeks seems to be the answer
- Does PrEP protect against other STIs?
 - No! (although there does seem to be data for ↓ HSV risk)

Case 2

- A 27 year old MSM in generally good health presents for care establishment. He has had a cold with fever, sore throat, and swollen glands for 2 days. He is taking frequent ibuprofen. He notably had unprotected anal sex with 1 primary and 2 occasional male partners (most recently about 10 days ago). He is interested in PrEP.
- Labs reveal a negative HIV antibody and negative HBsAg; Cr is normal

Case 2

- What's the next best step?
 - A. Start PrEP today
 - B. Wait until his cold has improved and he's off ibuprofen; then start PrEP
 - C. Start PEP, then transition to PrEP after 28 days
 - D. Send an HIV viral load and base the PrEP decision on the result

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Case 2, follow up

- His HIV viral load returns at 2.5 million copies/mL
- Acute HIV and PrEP
 - Remember that patients may be symptomatic from HIV but have negative serologic testing (i.e. in the “window period”)
 - In clinical trials of PrEP, drug resistant has been noted in those who were in the window period at enrollment
 - Use of the 4th generation antibody/antigen test decreases but does not eliminate the window period
 - If in doubt, SEND AN HIV RNA

Case 3

- A 48 year old man is presenting to clinic to establish care. He asks about obtaining PrEP as he is in a monogamous relationship with one male partner who is HIV-positive but virologically suppressed for over 5 years.
- Your patient's physical examination is unremarkable
- HIV antibody/antigen and HBsAg negative; Creatinine is 1.09 mg/dL
- He asks if PrEP is worthwhile for him since his partner is undetectable

Case 3

NO

- HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small

YES

- Viral rebound may occur because of poor ART adherence or other reasons
- People may not be monogamous
- CDC guidelines support PrEP in this context.

Case 3

- ART substantially reduces HIV transmission
 - HPTN 052 study: HIV treatment reduced HIV transmission by 96% in serodiscordant couples
 - IAS 2018: Zero transmissions after the HIV-infected partner was stably suppressed on ART in PARTNERS1 (heterosexuals) and PARTNERS2 (MSM)
 - Opposites Attract study: 0 HIV transmissions in 152 serodiscordant MSM couples despite ~6,000 episodes of condomless anal sex

- Cohen MS, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493-505.
- Grulich AE, et al. HIV in male serodiscordant couples in Australia, Thailand, and Brazil. CROI, 2015. Abstract 1019LB.
- Rodger A, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in MSM couples with suppressive ART: The PARTNER2 Study extended results in gay men. Program and abstracts of the 22nd International AIDS Conference; July 23-27, 2018; Amsterdam, the Netherlands. Abstract WEAX0104LB.

Case 4

- A 36 year old female and her 39 year old husband present to discussion conception. He is HIV-positive and virologically suppressed, and she is HIV-negative. They wish to conceive a child, and cannot afford sperm washing. They ask if you would recommend PrEP for her and condomless sex in this situation.

Case 4

- Would you agree with this approach?
 - A. Yes
 - B. No

Case 4

- PrEP may be a part of a conception strategy
- There is no evidence for increased birth defects with TDF-FTC among women in the Antiretroviral Pregnancy Registry (ART report)
- Other reproductive strategies for such couples may be limited to non-existent
- Notably, modeling suggests that PrEP adds little if ART and other factors are optimized (Hoffman)

Antiretroviral pregnancy registry interim report. 2014. Available from: www.apregistry.com/forms/exec-summary.pdf.

Hoffman RM, et al. Benefits of PrEP as an adjunctive method of HIV prevention during attempted conception between HIV-uninfected women and HIVinfected male partners. *J Infect Dis.* 2015;212(10):1534.

HIV PrEP: Future Directions

- More data is needed in women, adolescents, and youth (15-17 year olds currently being studied in ATN 113)
- Novel PrEP Agents are being evaluated
 - Tenofovir alafenamide (TAF) for PrEP (Pro-drug of TDF) has less effect on bone and mineral metabolism and renal function
 - Intramuscular injections of long-acting integrase inhibitors
 - Tenofovir vaginal ring
 - Long-acting TAF (GS-7340) subdermal implant
- Additional research is ongoing on different dosing regimens as well

Take Home Points

- Daily TDF-FTC substantially reduces the risk of HIV infection in individuals at high risk.
- Serious side effects are rare; renal function must be monitored periodically while on PrEP.
- Before starting PrEP, test for acute HIV if there are suggestive clinical signs of symptoms
- There is no evidence of adverse pregnancy outcomes among women who conceive on TDF-FTC

Questions?

