



PrEP Basics

Sarah R. Blevins, PharmD, BCIDP, AAHIVM
HIV Clinical Pharmacist
University of Kentucky HealthCare

Faculty Disclosure

- No financial disclosures

Educational Need/Practice Gap

Gap = Kentucky and much of the southeast United States have been identified as priority areas for the CDC's "Ending the Epidemic" campaign for HIV

Need = HIV pre-exposure prophylaxis is integral to ending the HIV epidemic; therefore, practitioners need the knowledge to safely and effectively provide PrEP for their patients

Expected Outcome

- Increased comfort level with providing HIV pre-exposure prophylaxis as part of routine clinical practice

Objectives

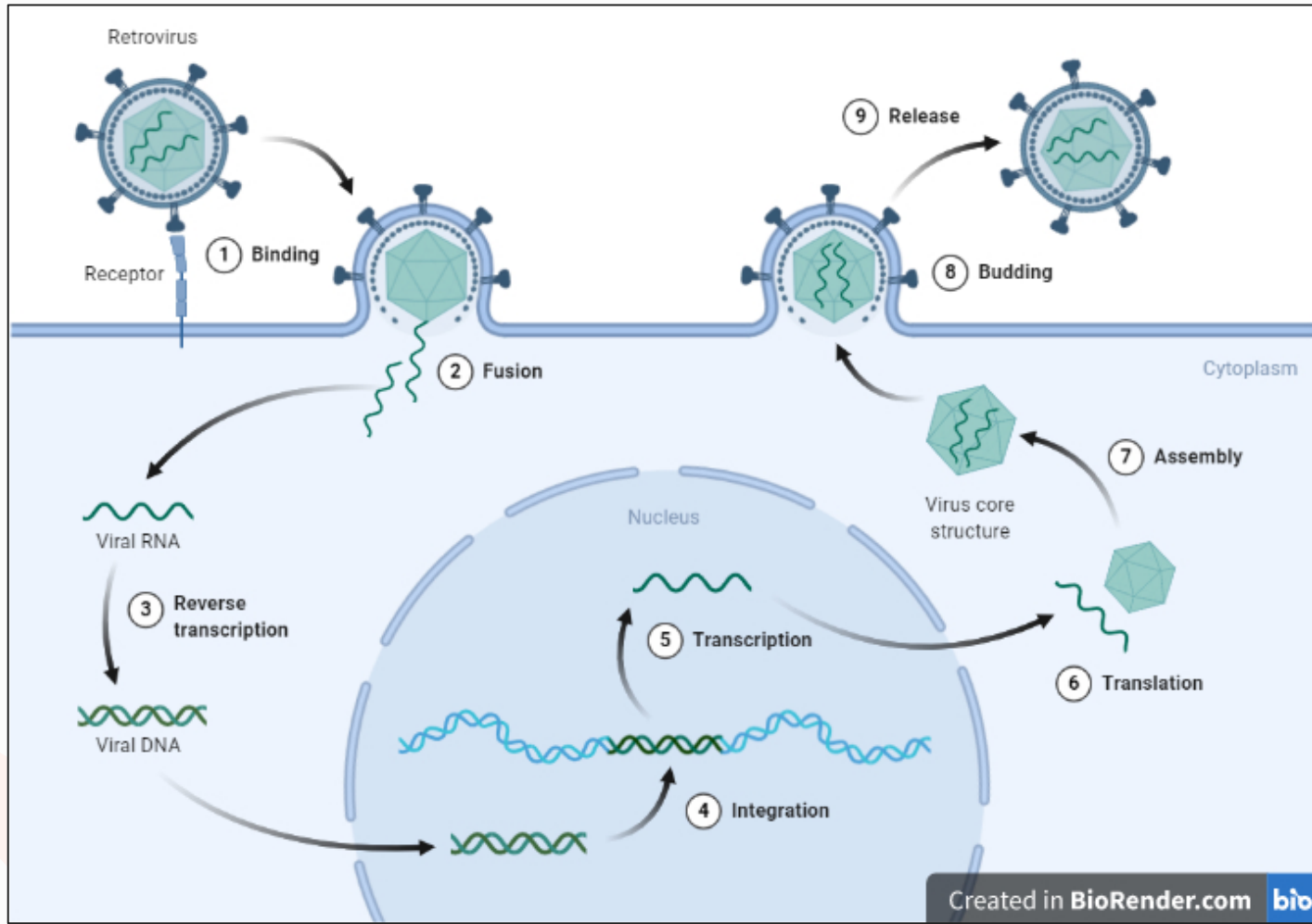
Upon completion of this educational activity, you will be able to:

- Review HIV pathophysiology and HIV epidemiology in the United States and Kentucky
- Describe risk factors for HIV acquisition
- Review data associated with HIV pre-exposure prophylaxis
- Discuss US Public Health Service Guidelines for HIV Pre-Exposure Prophylaxis
- Provide tools to implement PrEP program in your clinic

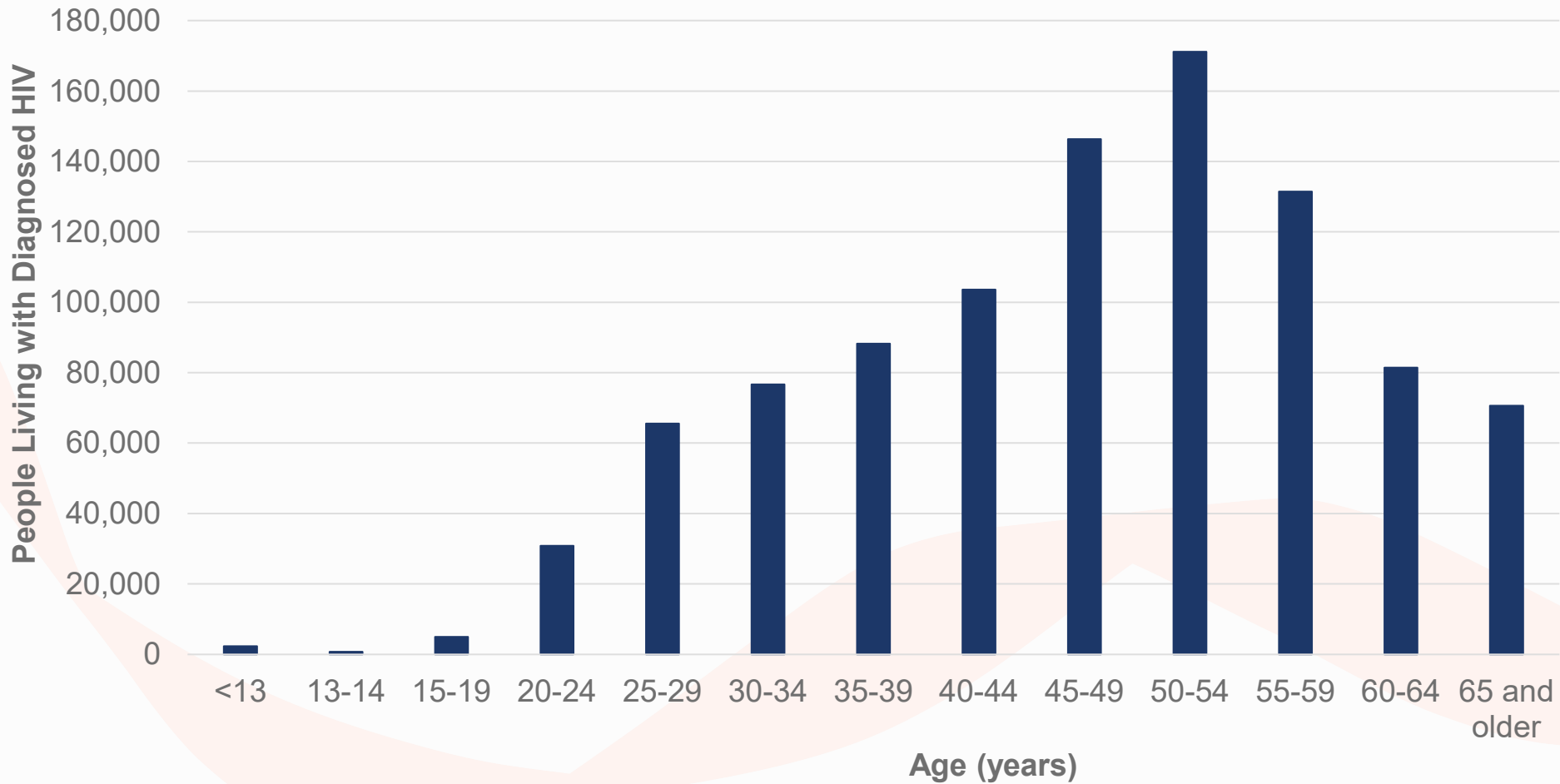
Abbreviations

- CrCl: creatinine clearance
- HAV: hepatitis A virus
- HBV: hepatitis B virus
- HPV: human papillomavirus
- IVDU: intravenous drug use
- MSM: men who have sex with men
- PrEP: pre-exposure prophylaxis
- SCr: serum creatinine
- STI: sexually transmitted infection
- TAF: tenofovir alafenamide fumarate
- TAF/FTC: tenofovir alafenamide fumarate/emtricitabine
- TDF: tenofovir disoproxil fumarate
- TDF/FTC: tenofovir disoproxil fumarate/emtricitabine

HIV Review

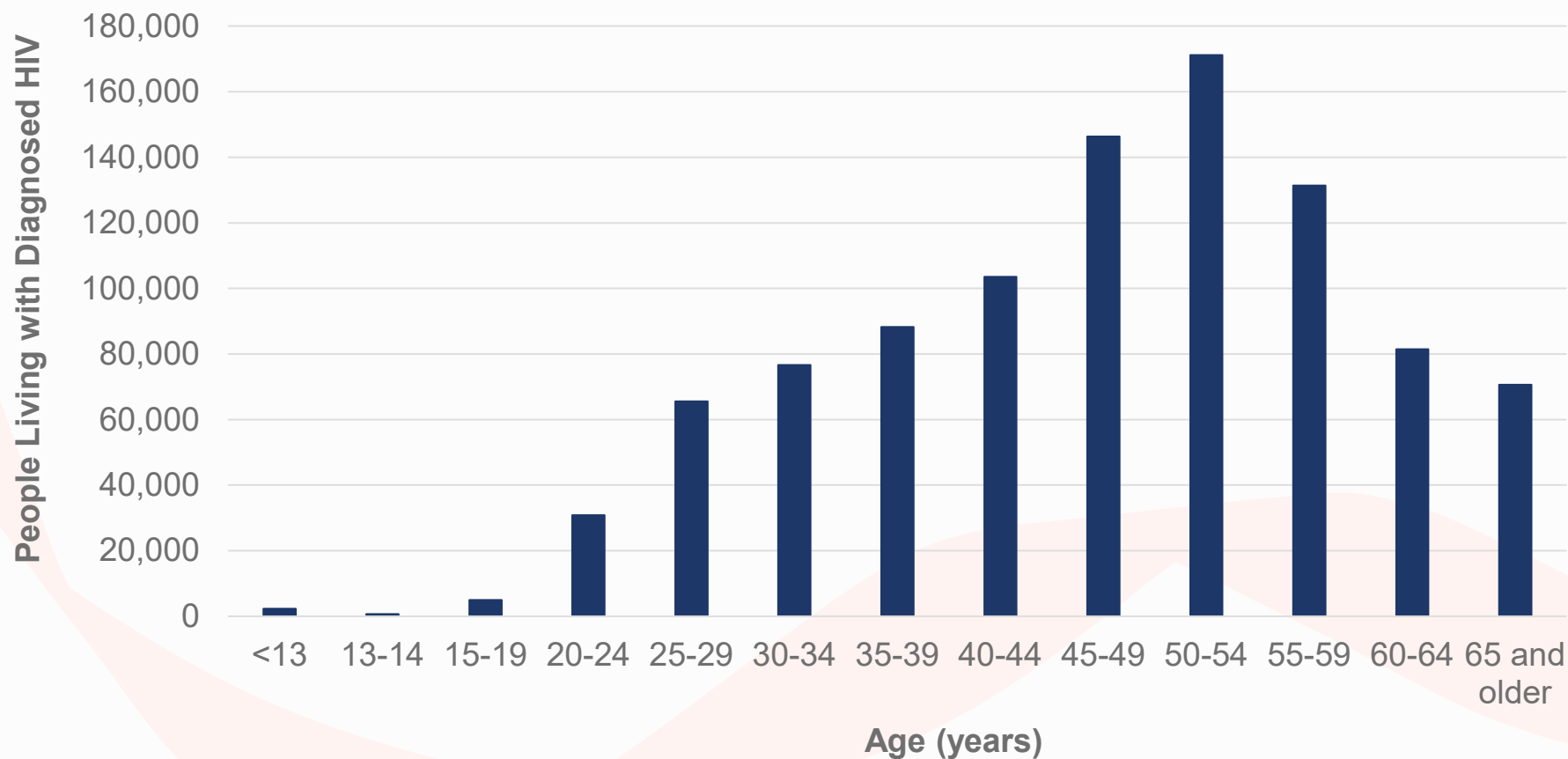


Age Distribution: People Living with HIV



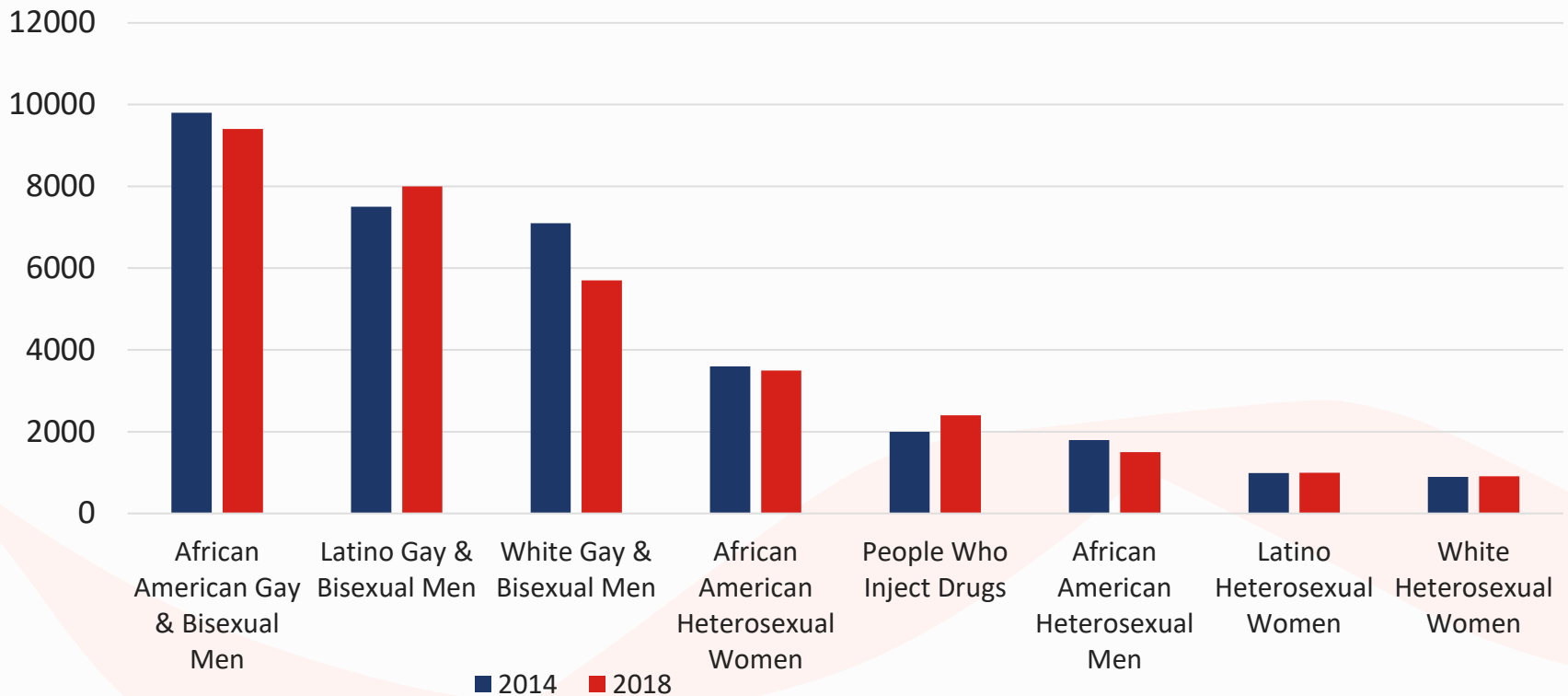
<https://www.cdc.gov/hiv/group/age/olderamericans/index.html>

Age Distribution: New HIV Diagnoses



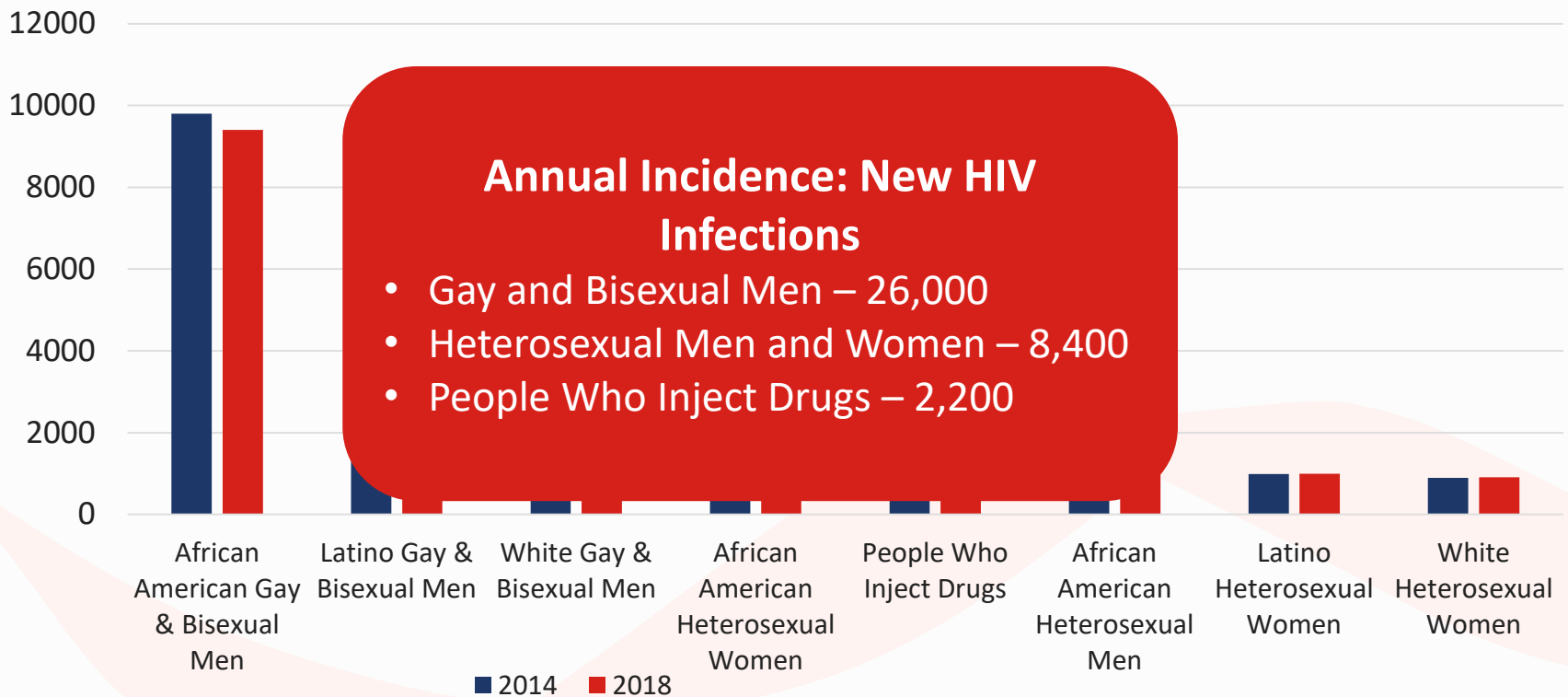
United States New HIV Diagnoses

New HIV Infections by Race and Transmission Group, 2014 vs. 2018



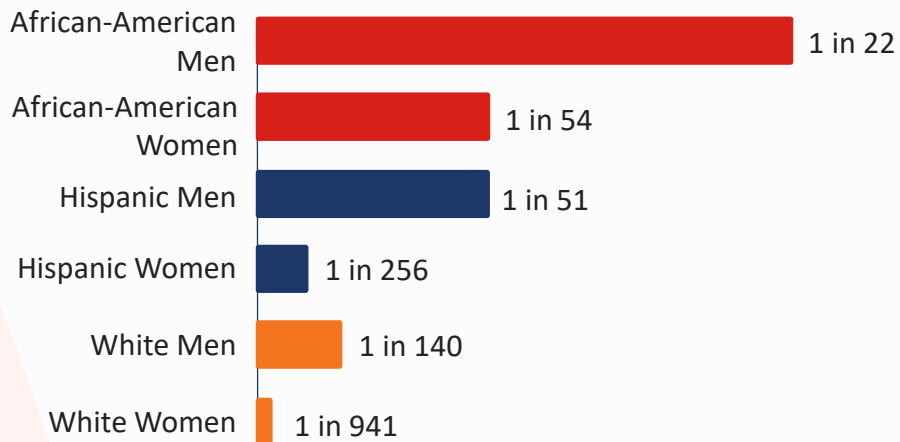
United States New HIV Diagnoses

New HIV Infections by Race and Transmission Group, 2014 vs. 2018

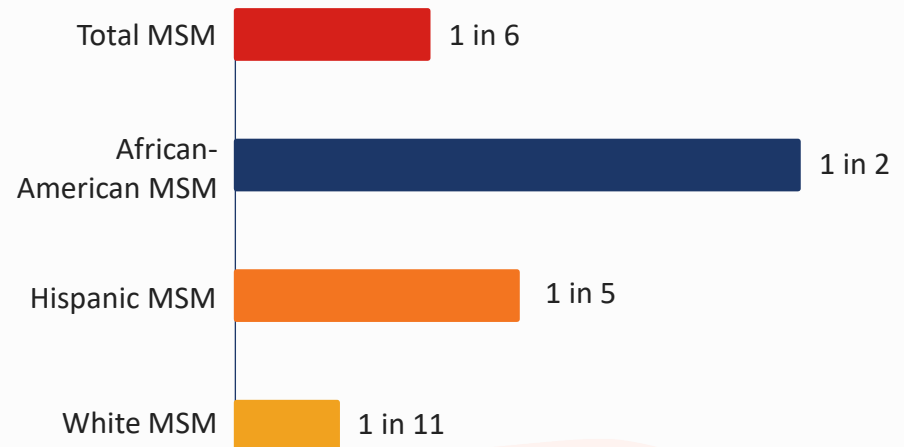


Lifetime Risk of HIV Diagnosis

Lifetime Risk of HIV Diagnosis by Race/Ethnicity

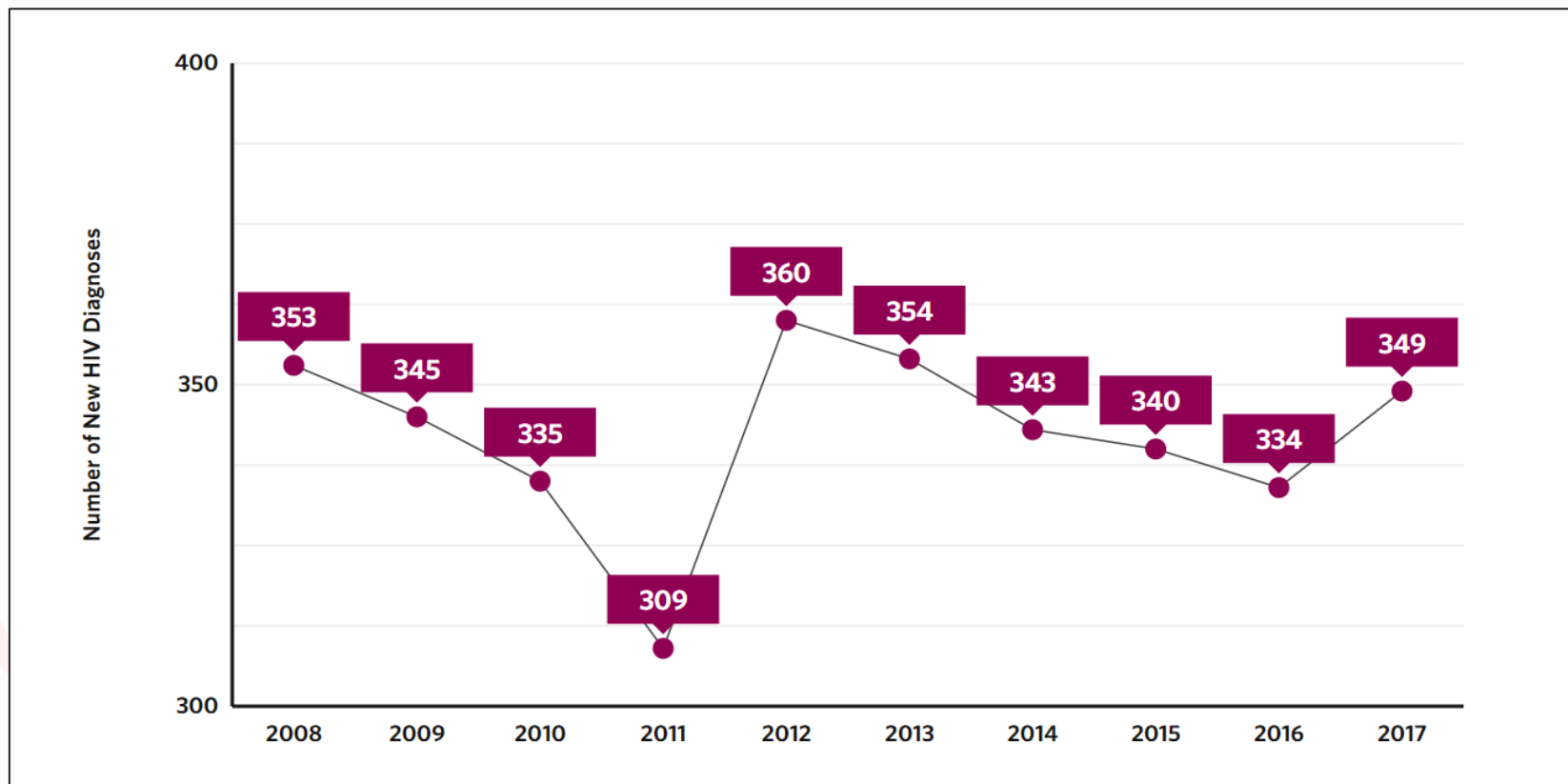


Lifetime Risk of HIV Diagnosis Among MSM by Race/Ethnicity

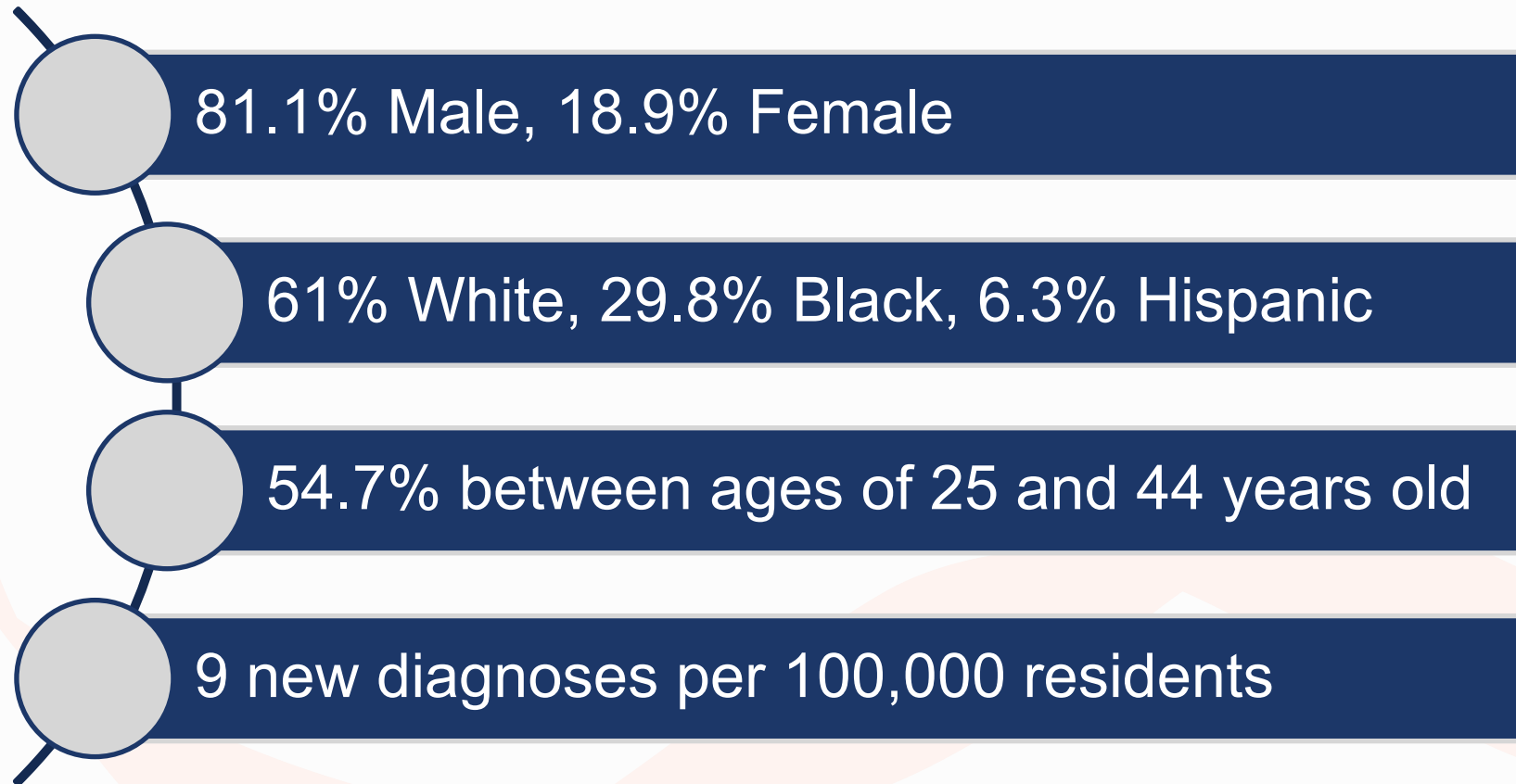


- The overall lifetime risk of HIV in the United States is 1 in 106
- African-American men have highest lifetime risk of HIV of all races and ethnicities (1 in 22)
- African-American MSM (1 in 2) and Hispanic MSM (1 in 5) have even higher lifetime risk of HIV
- Racial disparities along the HIV care continuum might reflect differences in access to and use of health care and treatment

Kentucky New HIV Diagnoses, 2008 – 2017



Kentucky New HIV Diagnoses - Demographics



Ending the Epidemic: A Plan for America

GOAL:

reaching
75%
reduction
in new HIV
infections
by 2025
and at least
90%
reduction
by 2030.



HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:



Diagnose all people with HIV as early as possible after infection.

Treat the infection rapidly and effectively to achieve sustained viral suppression.



Prevent new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).

Respond quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.



Ending the Epidemic: A Plan for America

GOAL:

reaching **75%** reduction in new HIV infections by 2025 and at least **90%** reduction by 2030.



HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:



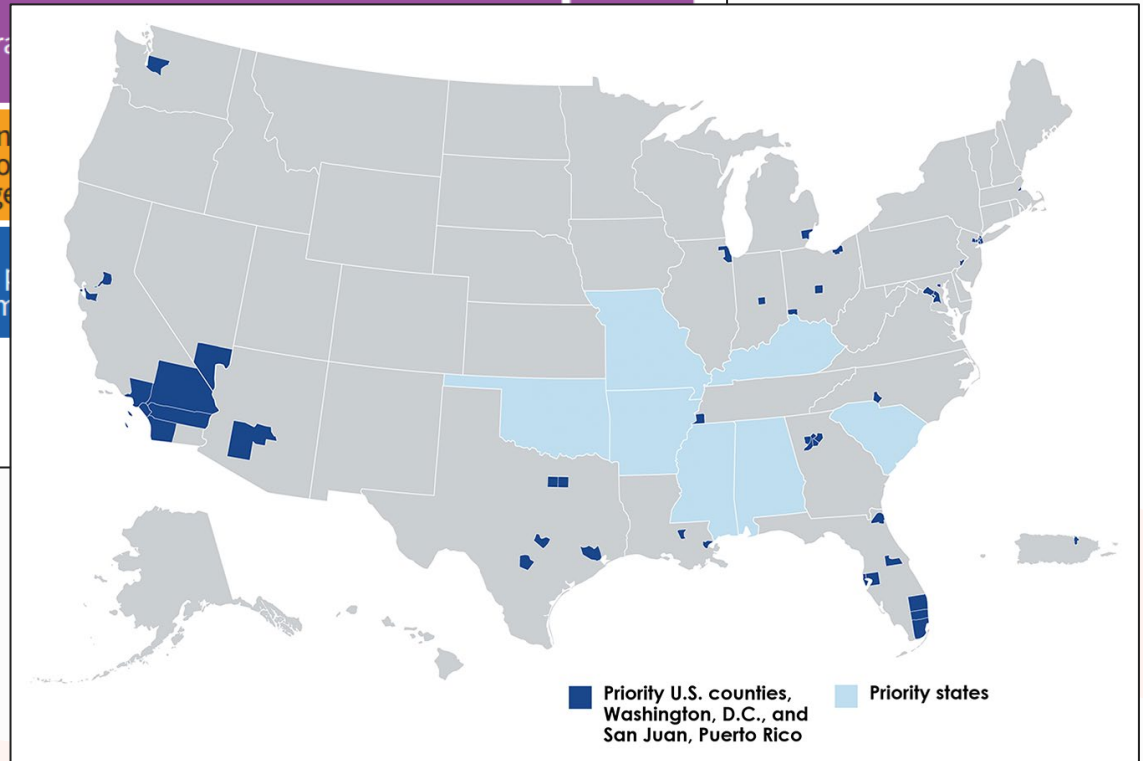
Diagnose all people with HIV as early as possible after infection.

Treat the infection rapidly to achieve viral suppression.

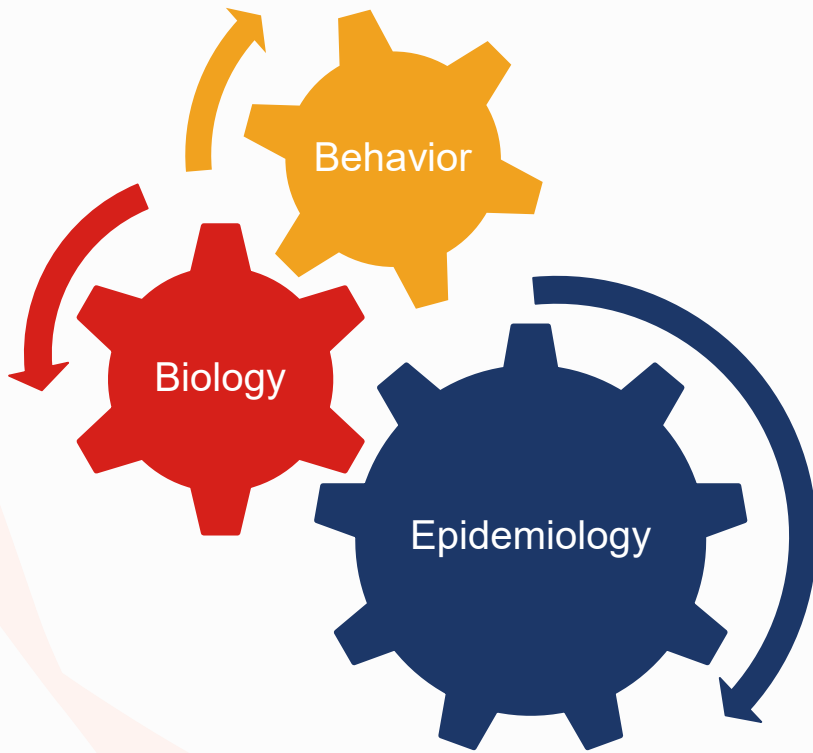


Prevent new infections through risk reduction interventions and syringe services.

Respond quickly to outbreaks through prevention and treatment.



Who's At Risk?



Behavior

- Condomless sex
- Sharing needles
- Exchanging sex for drugs or money

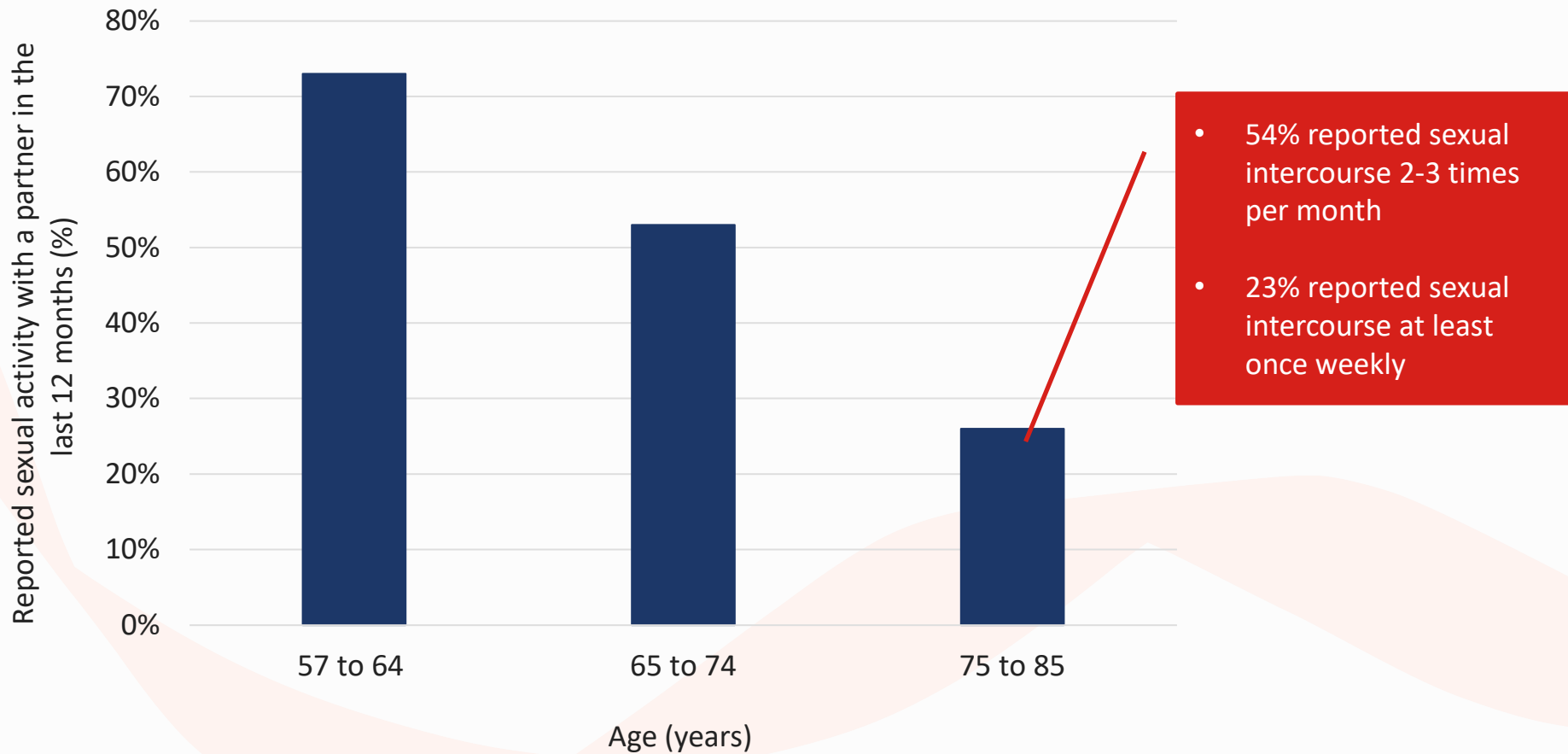
Biology

- Past or current STI
- Having partners of unknown HIV viremic status

Epidemiology

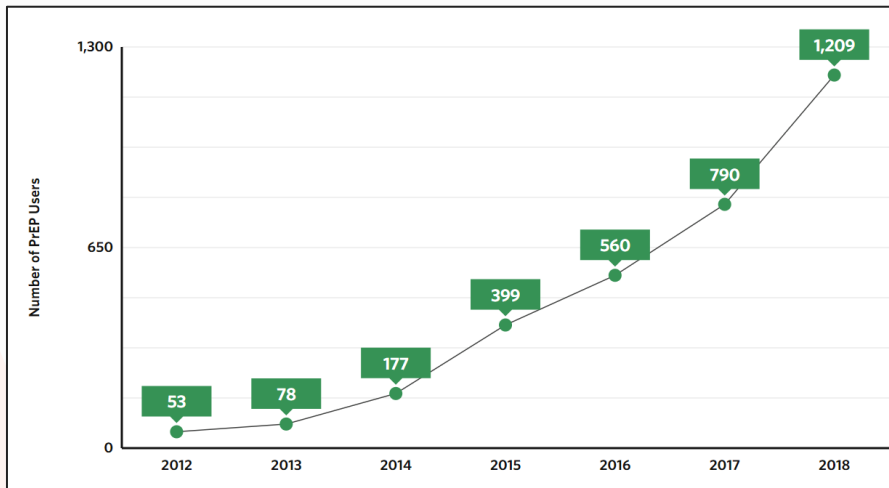
- Sexual activity in high prevalence area
- Sexual activity in high prevalence network

Prevalence of Sexual Activity in Older Adults

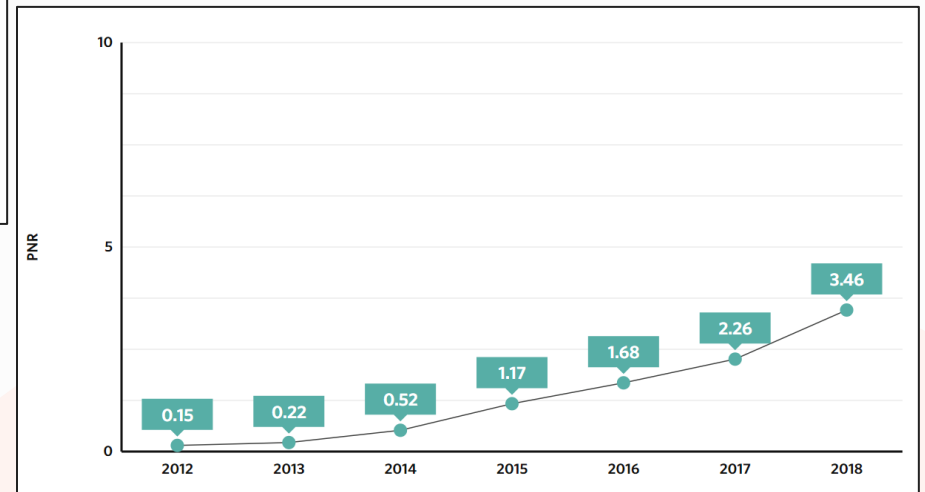


Kentucky – PrEP Need

Number of PrEP Users, 2012 - 2018



PrEP-to-Need (PNR), 2012 - 2018



Asking the Tough Questions

Factors that Facilitate a Sexual Health Conversation

Safe Environment	<ul style="list-style-type: none">• Ensure that the patient feels comfortable to discuss their sexual health• Allow for an open discussion about sexual health without passing judgement
Sex Positivity	<ul style="list-style-type: none">• Sex is good, healthy, and natural• Do not refer to sex as “risky” or discuss “risk behaviors”• Stigma related to adverse outcomes of sexual activity, may hinder both the seeking and provision of sexual health care
Build Trust	<ul style="list-style-type: none">• Use a sensitive and nonjudgmental tone• Avoid making assumptions based on the patients personal factors• Be sensitive and open to different sexual behaviors• If unaware of your patient’s gender identity, use gender-neutral word or language
Open-Ended Questions	<ul style="list-style-type: none">• Ask open-ended questions to encourage a discussion about the patient’s sexual health• Close-ended-questions can cause the patient to withhold information

PrEP = Pre-Exposure Prophylaxis

- Daily antiretroviral for prevention of HIV
- Two FDA-approved options
 - Truvada®
 - Tenofovir disoproxil fumarate/emtricitabine 300mg/200mg (TDF/FTC)
 - Descovy®
 - Tenofovir alafenamide fumarate/emtricitabine 25mg/200mg (TAF/FTC)
- The medications do not constitute a complete HIV regimen
- TDF and TAF are also indicated for the treatment of chronic HBV

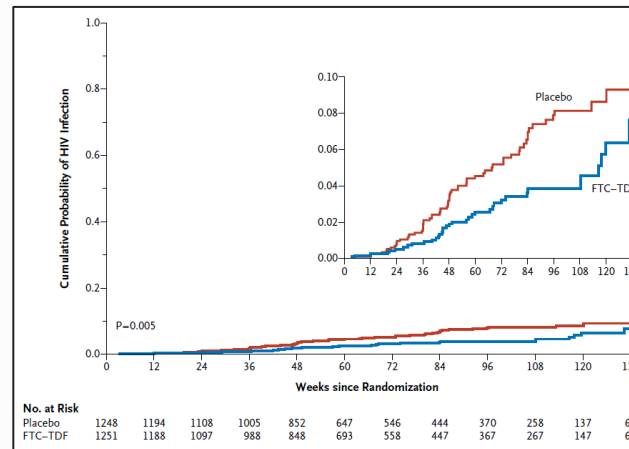
PrEP: The Evidence

Study	Design ^a	Participants		Limitations	Quality of Evidence (See Table 14, Appendix 2)
		Agent	Control		
Among Men Who have Sex with Men					
iPrEx Trial	Phase 3	TDF/FTC (n = 1251)	Placebo (n = 1248)	Adherence	High
US MSM Safety Trial	Phase 2	TDF (n = 201)	Placebo (n = 199)	Minimal	High
ATN 082	Pilot	TDF/FTC (n=20)	Placebo (n=19) No pill (n=19)	Small size, stopped early, limited follow-up time, low medication adherence	Low
Among Heterosexual Men and Women					
Partners PrEP	Phase 3	TDF (n = 1589) TDF/FTC (n = 1583)	Placebo (n = 1586)	Minimal	High
TDF2	Phase 2	TDF/FTC (n = 611)	Placebo (n = 608)	High loss to follow-up; modest sample size	Moderate
Among Heterosexual Women					
FEM-PrEP	Phase 3	TDF/FTC (n = 1062)	Placebo (n = 1058)	Stopped at interim analysis, limited follow-up time; very low adherence to drug regimen	Low
West African Trial	Phase 2	TDF (n = 469)	Placebo (n = 467)	Stopped early for operational concerns; small sample size; limited follow-up time on assigned drug	Low
VOICE	Phase 2B	TDF (n = 1007) TDF/FTC (n = 1003)	Placebo (n = 1009)	TDF arm stopped at interim analysis (futility); very low adherence to drug regimen in both TDF and TDF/FTC arms	Low
Among Injection Drug Users					
BTS	Phase 3	TDF (n = 1204)	Placebo (n = 1207)	Minimal	High

iPREX (Pre-exposure Prophylaxis Initiative) Trial

Grant RM, Lama JR, Anderson PL et al. *N Engl J Med* 2010; 363:2587-2599

- TDF/FTC vs. placebo
- Inclusion criteria
 - Male sex at birth
 - ≥ 18 years old
 - HIV negative
- Study visits
 - Drug dispensation
 - Pill count
 - Adherence counseling
 - Rapid HIV test
- Labs



- HIV acquisition
 - Placebo: 64
 - TDF/FTC: 36
 - 44% risk reduction
 - P = 0.005

What About Adherence?

- $\geq 50\%$ adherence = 50% risk reduction
- $\geq 90\%$ adherence = 73% risk reduction

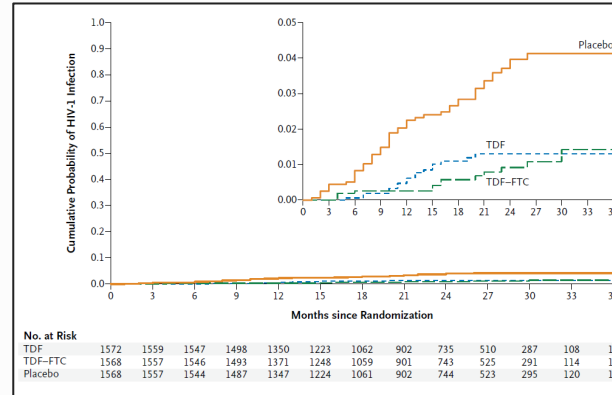
Adverse Effects

- TDF/FTC more likely to cause nausea and unintended weight loss (P=0.04)
- More SCr elevations in TDF/FTC group (P=0.08)

Partners PrEP Study

Baeten JM, Donnell D, Ndase P et al. *N Engl J Med* 2012;367:399-410

- TDF vs. TDF/FTC vs. placebo
- Inclusion criteria
 - Serodiscordant heterosexual couples
 - HIV negative partner
 - Normal renal function
 - HBV negative
 - Not pregnant or breastfeeding
 - HIV positive partner
 - Not on antiretroviral therapy
- Study visits
 - Drug dispensation
 - Pill count
 - Adherence counseling
 - Rapid HIV test
- Labs



• HIV Acquisition

- Placebo: 52
- TDF: 17
- TDF/FTC: 13
- TDF risk reduction: 67% (P < 0.001)
- TDF/FTC risk reduction: 75% (P < 0.001)

- HIV negative partner was male in 61% of couples
- Protective effect of TDF or TDF/FTC was not different between men and women

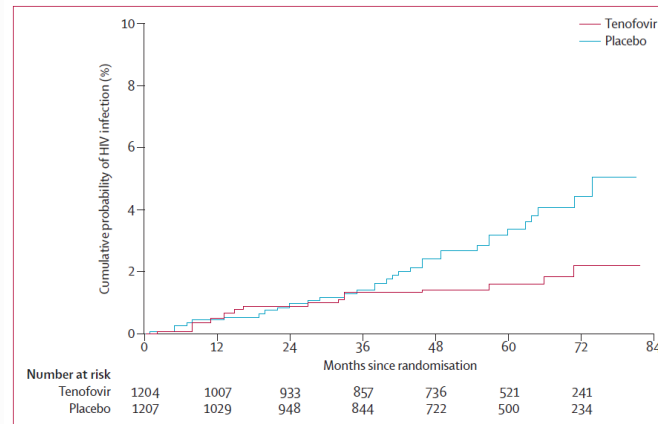
Adverse Effects

- No significant difference in adverse effects
- GI distress more common in TDF and TDF/FTC groups

Bangkok Tenofovir Study

Choopanya K, Martin M, Suntharasamai P, et al. *Lancet* 2013 Jun 15;381(9883):2083-90

- TDF vs. placebo
- Inclusion criteria:
 - 20 – 60 years old
 - Injection drug use
- Exclusion criteria:
 - HBV
 - Pregnant or breastfeeding
- Participants chose DOT or monthly visits
- Labs



- HIV acquisition
 - Placebo: 35
 - TDF: 17
 - 51.8% risk reduction
 - P = 0.01

IV Drug Use

- Heroin
- Methamphetamine
- Midazolam
- ~22% were in a methadone program

Adverse Effects

- TDF more likely to cause nausea (P = 0.002)
- No difference in SCr elevation

DISCOVER: TAF/FTC vs. TDF/FTC for PrEP

Hare CB, Coll J, Ruane P et al. Presented at 2019 Conference on Retroviruses and Opportunistic Infections

- TAF/FTC vs. TDF/FTC
- Inclusion criteria
 - Men and transgender women
 - ≥ 2 acts of condomless anal sex in past 12 weeks
- OR
- Rectal gonorrhea/chlamydia or syphilis in past 24 weeks
- HIV Acquisition
 - TAF/FTC: 8
 - TDF/FTC: 15
 - IRR: 0.54; 95% CI: 0.23 – 1.26
 - Non-inferior

Renal Safety

- TAF/FTC had fewer cases of treatment emergent proteinuria (P=0.03) and SCr increases (P<0.001)

Bone Mineral Density

- Lumbar Spine
 - TDF/FTC: ↓1.39%
 - TAF/FTC: ↑0.95%
 - P < 0.001
- Hip
 - TDF/FTC: ↓1.01%
 - TAF/FTC: ↑0.15%
 - P < 0.001

DISCOVER: TAF/FTC vs. TDF/FTC for PrEP

Hare CB, Coll J, Ruane P et al. Presented at 2019 Conference on Retroviruses and Opportunistic Infections

- TAF/FTC vs. TDF/FTC

- Inclusion criteria

- Men and transgender women
- ≥ 2 acts of condomless anal sex in past 12 weeks
- OR

- Rectal gonorrhea/chlamydia or syphilis in past 24 weeks

- HIV Acquisition

TAF/FTC vs. TDF/FTC

0.23 –

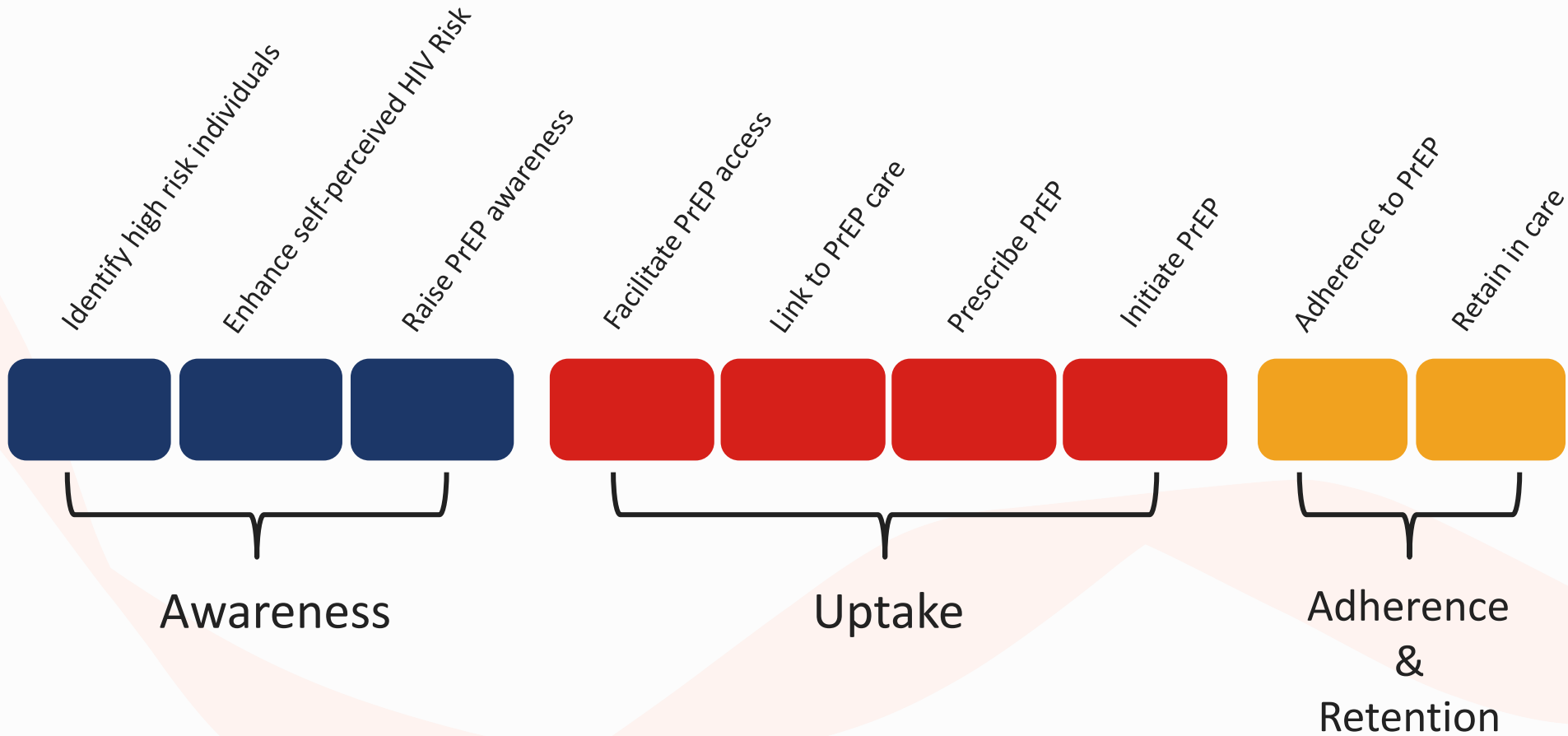
Not approved for individuals who have receptive vaginal sex

fewer cases of treatment emergent proteinuria (P=0.03) and SCr increases (P<0.001)

Bone Mineral Density

- Lumbar Spine
 - TDF/FTC: ↓1.39%
 - TAF/FTC: ↑0.95%
 - P < 0.001
- Hip
 - TDF/FTC: ↓1.01%
 - TAF/FTC: ↑0.15%
 - P < 0.001

PrEP Care Continuum



PrEP Care Continuum: Awareness

Identify high risk individuals
Enhance self-perceived HIV Risk
Raise PrEP awareness

Facilitate PrEP access

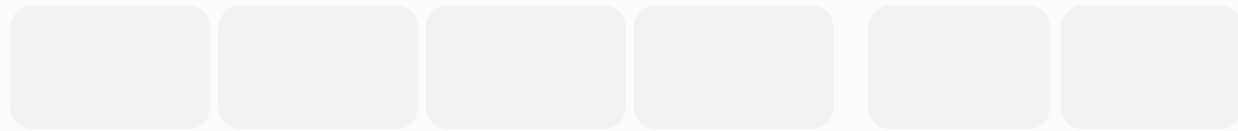
Link to PrEP care

Prescribe PrEP

Initiate PrEP

Adherence to PrEP

Retain in care



Awareness



Uptake

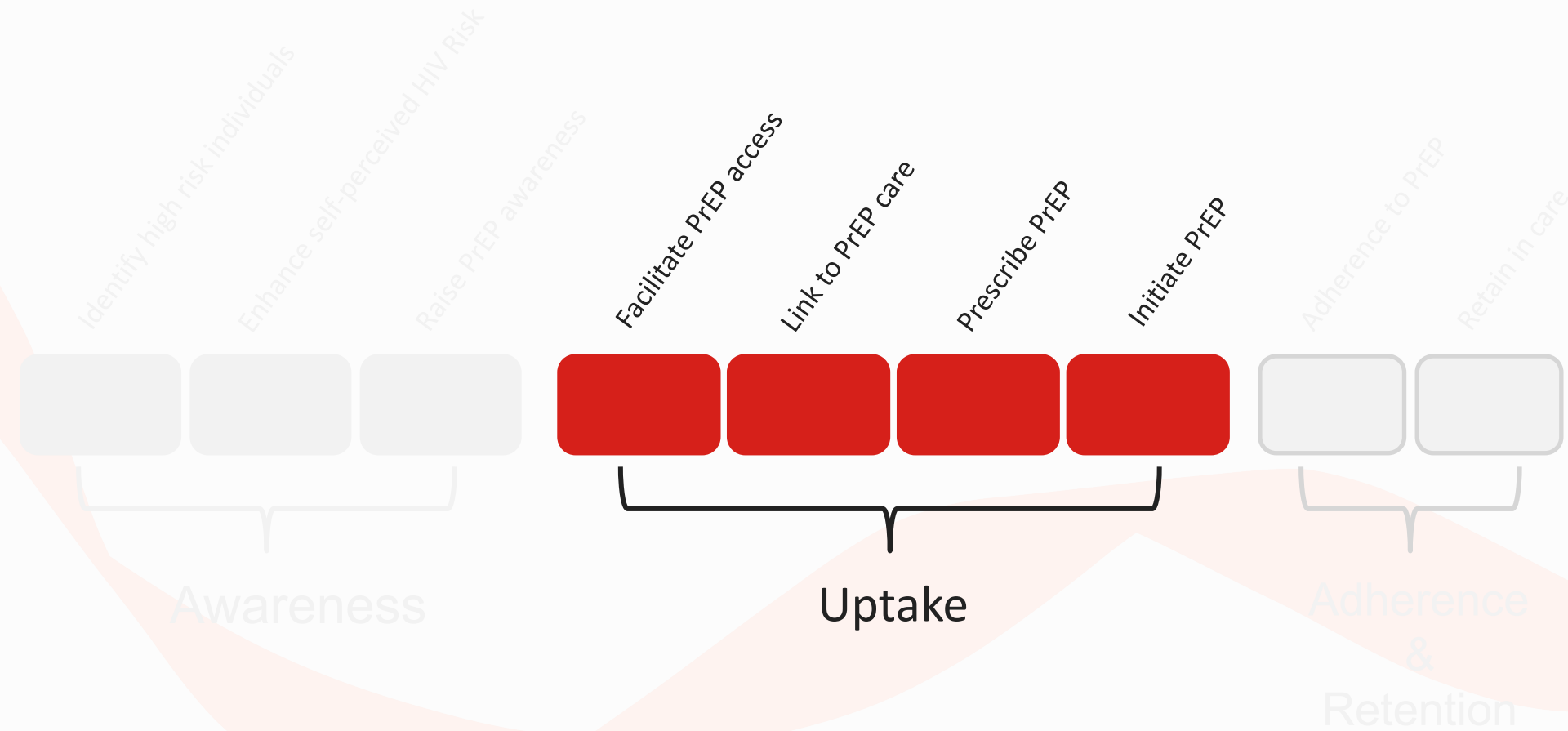


Adherence
&
Retention

Identifying High Risk Patients

MSM	Heterosexual Men and Women	People Who Inject Drugs
<ul style="list-style-type: none"> • Adult male • Without acute or established HIV infection • Any male partners in past 6 months • Not in a monogamous partnership with a recently tested, HIV-negative man 	<ul style="list-style-type: none"> • Adult person • Without acute or established HIV infection • Any sex with opposite sex partners in past 6 months • Not in a monogamous partnership with a recently tested, HIV-negative partner 	<ul style="list-style-type: none"> • Adult person • Without acute or established HIV • Any injection of drugs not prescribed by a clinician in the past 6 months
<p><u>And ≥ 1 of the following:</u></p> <ul style="list-style-type: none"> • Any anal sex (receptive or insertive) without condoms in the past 6 months • A bacterial STI diagnosed or reported in past 6 months 	<p><u>And ≥ 1 of the following:</u></p> <ul style="list-style-type: none"> • Is a man who has sex with men and women • Infrequent condom use with ≥1 high risk partner • Ongoing sexual relationship with HIV positive partner • A bacterial STI diagnosed or reported in past 6 months 	<p><u>And ≥ 1 of the following:</u></p> <ul style="list-style-type: none"> • Any sharing of injection or drug preparation equipment in the past 6 months • Risk of sexual acquisition

PrEP Care Continuum: Uptake



Baseline Labs

Baseline Lab/Assessment		Timing	
		TAF/FTC	TDF/FTC
HIV ^{1,2}	<ul style="list-style-type: none"> Screen all individuals for HIV-1 infection immediately prior to initiating PrEP 	Prior to initiation	Prior to initiation
HBV ^{1,2}	<ul style="list-style-type: none"> Prior to or when initiating PrEP, test patients for hepatitis B virus infection <ul style="list-style-type: none"> HBV-uninfected individuals should be offered vaccination If appropriate, anti-hepatitis B therapy may be warranted 	Prior to Initiation or when initiating	Prior to Initiation or when initiating
Renal Function ^{1,2}	<ul style="list-style-type: none"> Serum creatinine, estimated creatinine clearance, urine glucose and urine protein. In patients with Chronic Kidney Disease, also assess serum phosphorous 	Prior to Initiation or when initiating	Prior to initiation
STIs ³	<ul style="list-style-type: none"> Screen for genital, oral, and rectal STIs 	At Baseline	At Baseline
Hepatitis C ^{3,4}	<ul style="list-style-type: none"> All sexually active individuals initiating PrEP should be tested for HCV infection 	At Baseline	At Baseline
Pregnancy Test	<ul style="list-style-type: none"> As appropriate 	N/A	If appropriate

Confirming HIV Status

- Initial screening for HIV should be with a rapid or laboratory-based 4th generation HIV test (HIV1/2 antibody + p24 antigen)
- Do not screen with oral fluid tests
- If the screening test is negative, assess for acute HIV Infection
- If any signs and symptoms of acute HIV infection in the last 4 weeks, screen for acute infection using a test FDA-approved for this purpose (HIV NAAT test or HIV viral load)
 - If negative, OK to start PrEP
 - If positive, link to care for HIV treatment

Signs and Symptoms of Acute HIV

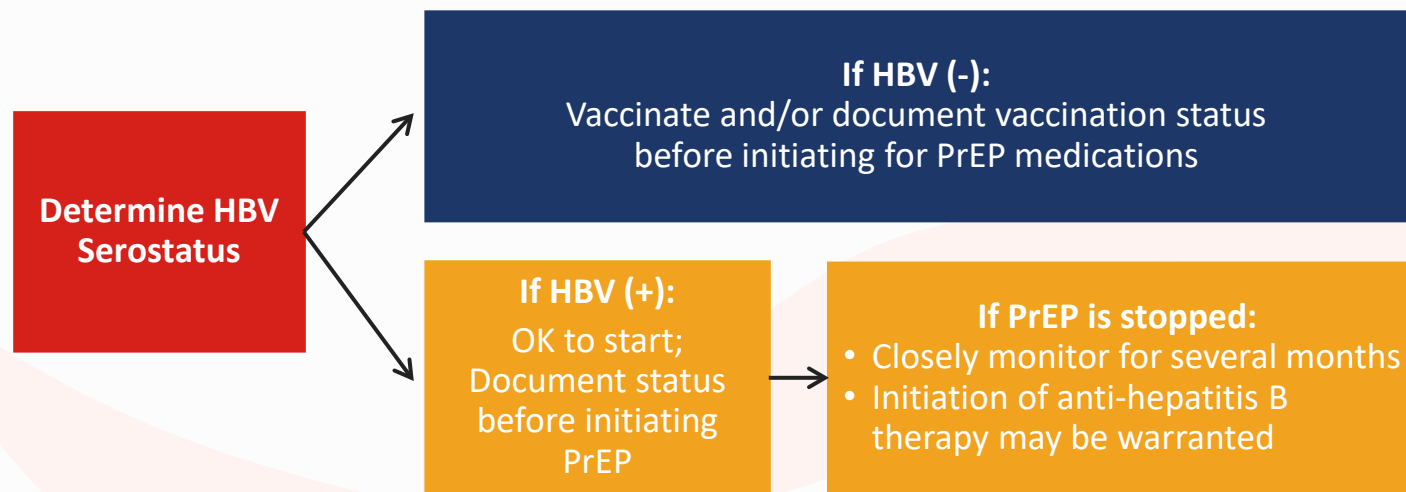
Sore Throat	Fatigue	Fever
Lymphadenopathy	Tonsillitis	Diarrhea
Myalgia	Arthralgia	Rash

HIV Drug Resistance

Trial	Trial Arm	Individuals with unrecognized acute HIV-1 infection at initiation		Individuals infected with HIV-1 after initiation	
		Total number of HIV (+) individuals	Number of HIV (+) individuals with resistance to a component of FTC/TFV	Total number of HIV (+) individuals	Number of HIV (+) individuals with resistance to a component of FTC/TFV
Partners PrEP	Placebo	6	0	52	0 ^b
	FTC/TDF or TDF	8	2	30	0 ^b
iPrEX	Placebo	8	1	64 ^c	0
	FTC/TDF	2	2	36 ^c	0
DISCOVER *	FTC/TAF	1	0 ^d	6	0 ^d
	FTC/TDF	4	4	11	0 ^d

Hepatitis B Exacerbations

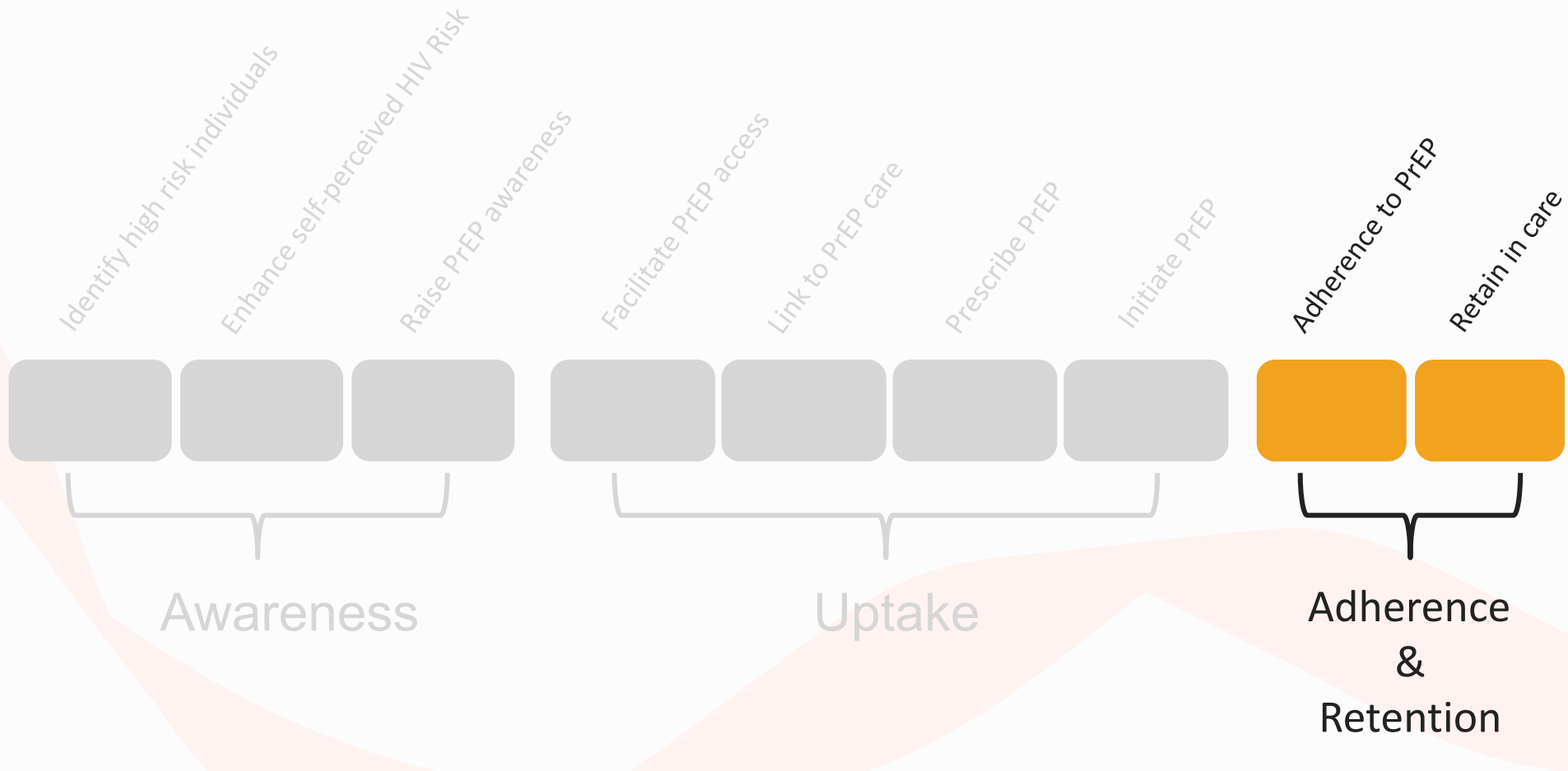
- Severe acute exacerbations of HBV have been reported in patients co-infected with HIV-1 and HBV who are taking products containing FTC and/or TDF
- This may also occur with discontinuation of TAF/FTC or TDF/FTC for PrEP



Other Considerations

-
- Education to maximize safe use
 - Medication adherence support
 - Provide contraception for women who do not wish to become pregnant
 - Vaccinations: HPV, HBV, HAV
 - Risk reduction: condoms, naloxone, safe injection practices

PrEP Care Continuum: Adherence and Retention



Follow-Up

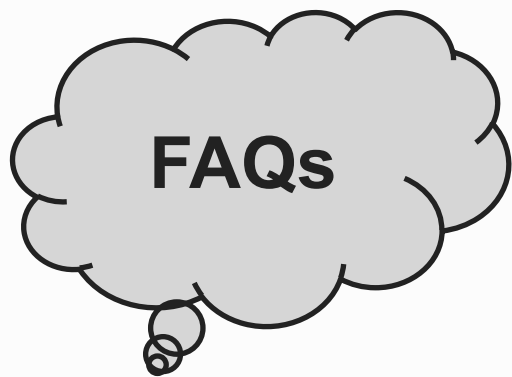
Every 3 Months	Every 6 Months	Every 12 Months	Optional
<ul style="list-style-type: none"> • HIV Test • Assess for signs and symptoms of acute HIV • Pregnancy test • Assess adherence, side effects, etc. • Testing for those with s/sx of bacterial STI • STI screening for MSM with high risk for recurrent infection • Provide PrEP prescription for no more than a 90 day supply 	<ul style="list-style-type: none"> • Check SCr and estimated creatinine clearance • May need more frequent monitoring or urinalysis if clinically indicated • STI screening for all patients whether they are asymptomatic or not • A rise in SCr is not a reason to withhold PrEP if: <ul style="list-style-type: none"> • CrCl >60 mL/min on TDF/FTC • CrCl >30 mL/min on TAF/FTC 	<p>Evaluate need to continue PrEP as part of HIV prevention</p>	<ul style="list-style-type: none"> • DEXA Scan • Therapeutic Drug Monitoring

PrEP: New Directions



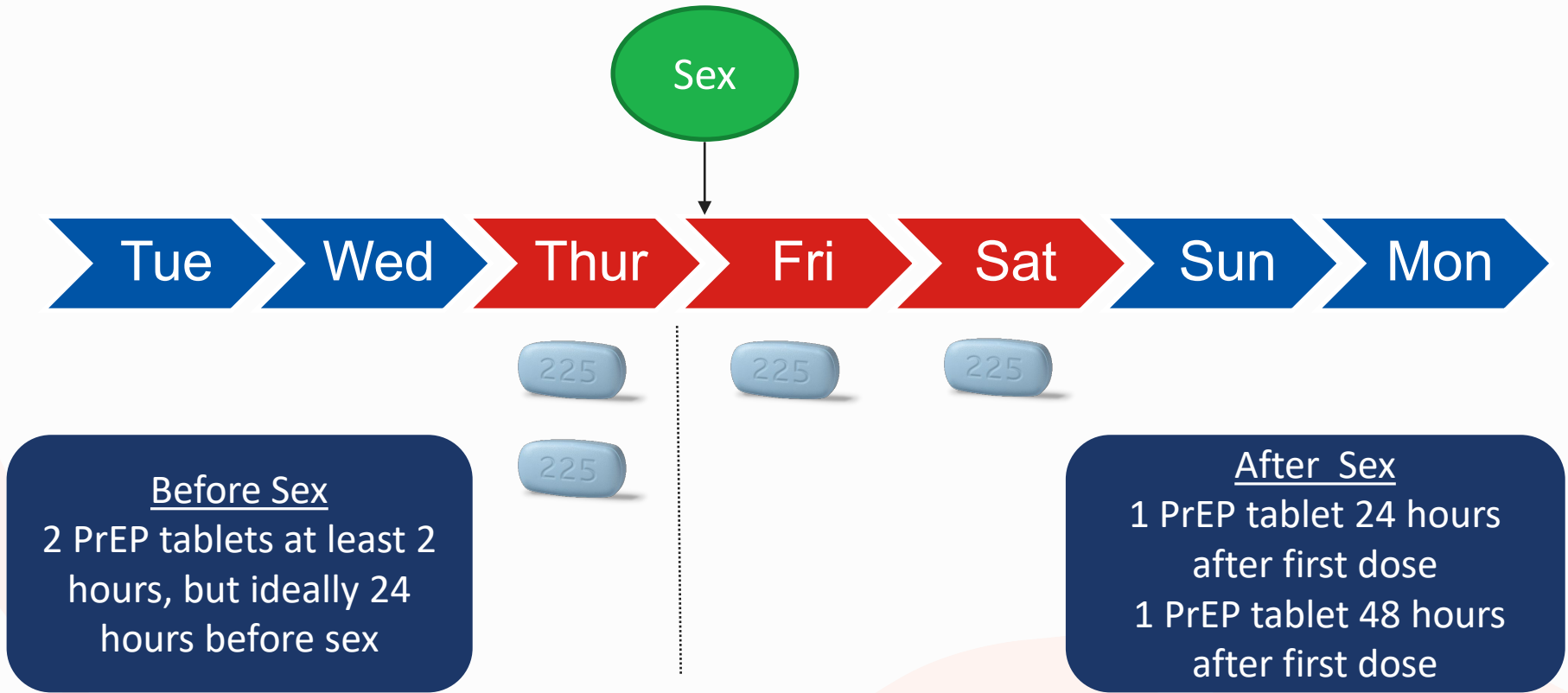
Cabotegravir

- Intramuscular injection
 - Every 8 weeks
- Superior to TDF/FTC



- How long do I have to take PrEP until it is effective?
 - Blood/Vaginal Tissue – 20 days
 - Rectal Tissue – 7 days
- What side effects will I have?
 - GI upset and headache are most common
- How many doses do I have to take to be protected?
 - All of them! In all seriousness, the more you take the more likely you will prevent infections
- I don't have to use condoms now, right?
 - While using a condom is your personal choice, you should know that PrEP does not protect you from other STIs or pregnancy
- What if I become pregnant?
 - It's ok to continue PrEP while pregnant (TDF/FTC only)
- I saw this ad for a lawsuit about Truvada® . . .
 - This has to do with patenting of Descovy® and Truvada® . Please don't hire an attorney. You won't get any money.

On Demand or Event Driven



If sexual activity continues, must take 1 PrEP tablet every 24 hours until 48 hours after last sex

PrEP Provider Resources



U.S. PHS/CDC Clinical Practice Guidelines for PrEP

<http://www.cdc.gov/hiv/risk/prep/index.html>



HIV Prevention Capacity Building Assistance Providers

www.cbaproviders.org



HRSA-funded AIDS Education and Training Centers

aidsetc.org



PrEPLine @ UCSF Clinical Consultation Center

855-448-7737 or 855 HIV-PrEP



NACCHO's PrEP for Local Health Departments Educational Series

<https://www.naccho.org/programs/community-health/infectious-disease/hiv-sti/prep-1/prep>



NASTAD PrEP Cost Calculator

www.PrEPcost.org

Questions?

- sarah_blevins@uky.edu