

PrEP for PWID: Challenges and Opportunities

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Objectives

1

Describe the epidemiology of HIV among people who inject drugs.

2

List evidence supporting PrEP for PWID and current CDC recommendations.

3

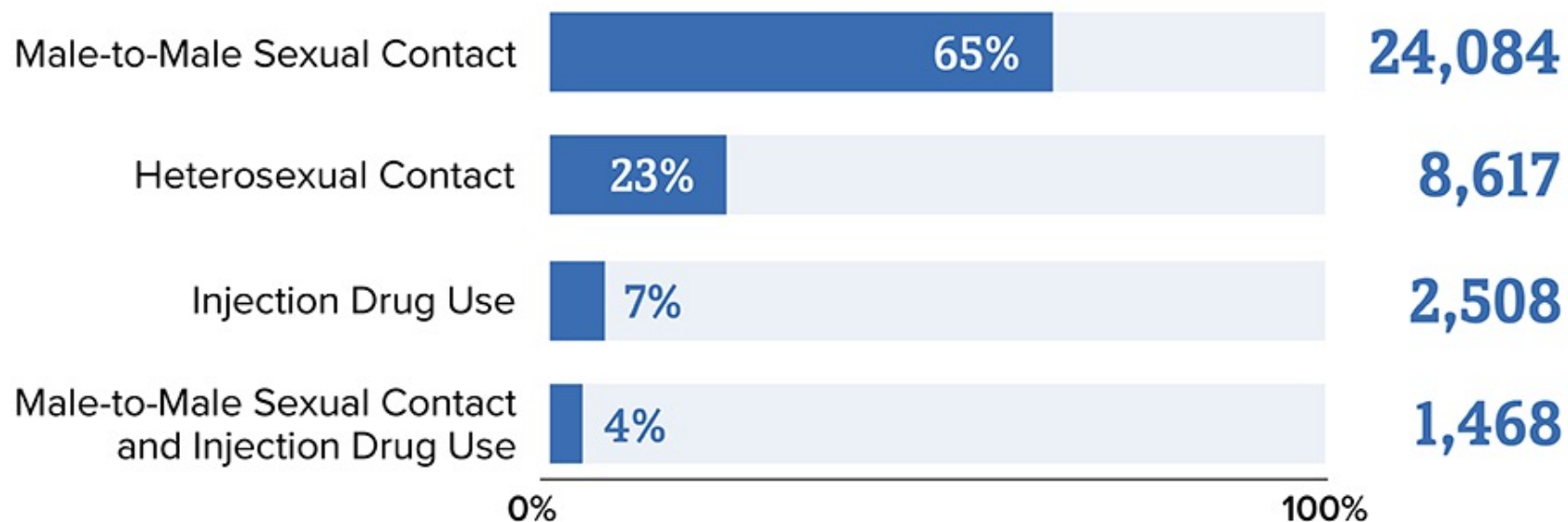
Outline challenges in the implementation of PrEP for PWID.

4

Describe future directions for delivery of PrEP for PWID.

Epidemiology of HIV among PWID

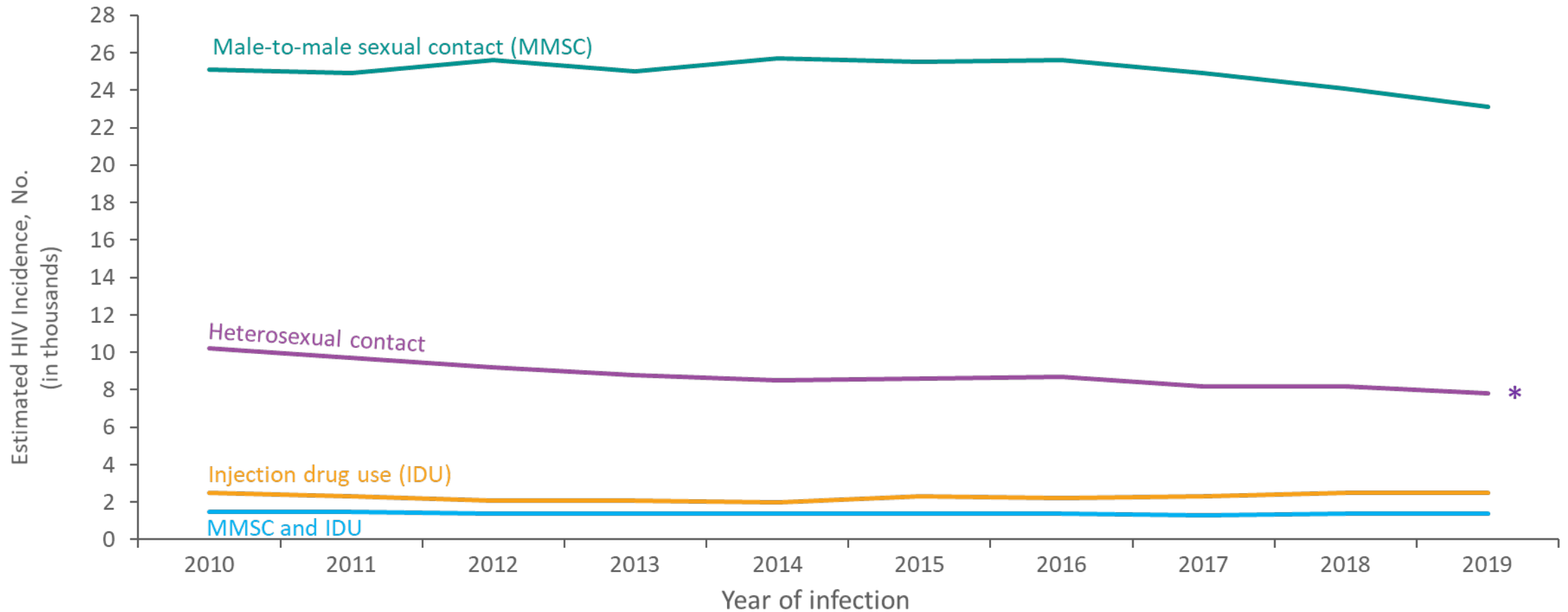
New HIV Diagnoses in the US and Dependent Areas by Transmission Category, 2019



NOTE: Does not include *other* and *perinatal* transmission categories.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

Estimated HIV Incidence among Persons Aged ≥13 Years, by Transmission Category 2010–2019—United States



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Data have been statistically adjusted to account for missing transmission category. Heterosexual contact is with a person known to have, or with a risk factor for, HIV infection.
* Difference from the 2010 estimate was deemed statistically significant ($P < .05$).



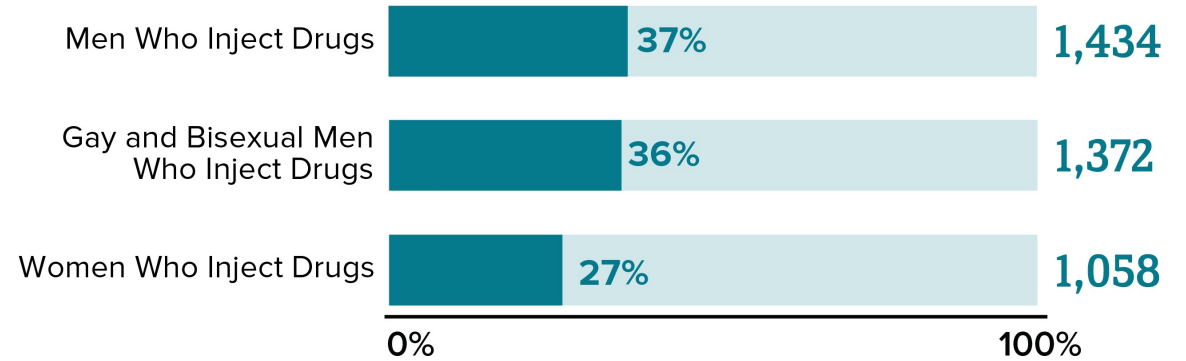


* Does not include MSM who inject drugs

Figure 1. Human immunodeficiency virus outbreaks among persons who inject drugs (United States, 2016–2019). Abbreviations: MSM, men who have sex with men; PWID, persons who inject drugs.

New HIV Diagnoses Among People Who Inject Drugs in the US and Dependent Areas by Sex, 2018*

Among people who inject drugs, most new HIV diagnoses were among men.

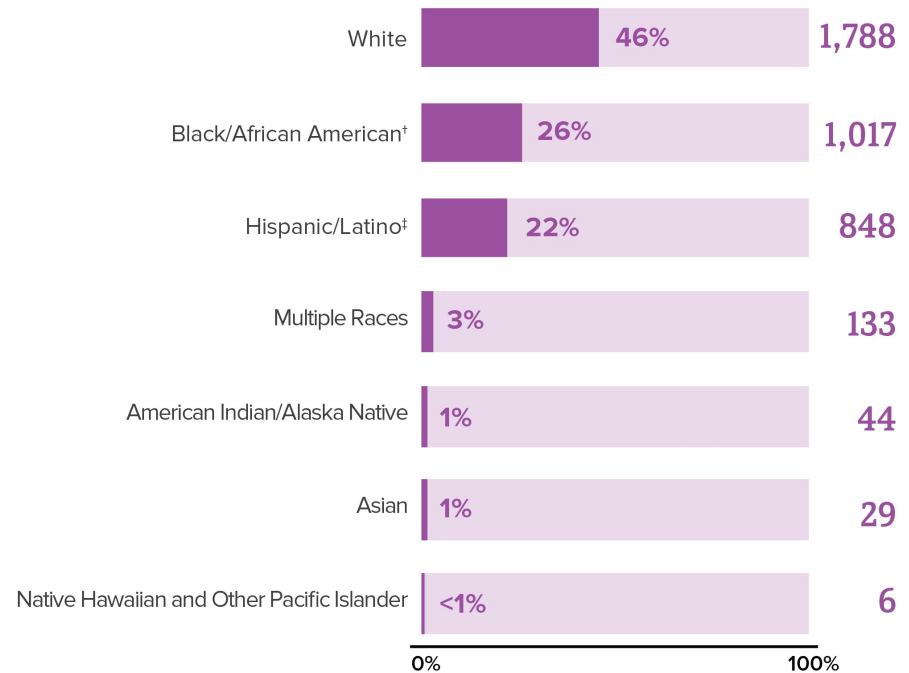


* Based on sex assigned at birth and includes transgender people.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

New HIV Diagnoses Among People Who Inject Drugs in the US and Dependent Areas by Race/Ethnicity, 2018*

White people accounted for the highest number of new HIV diagnoses among people who inject drugs.



* Includes infections attributed to male-to-male sexual contact *and* injection drug use (men who reported both risk factors).

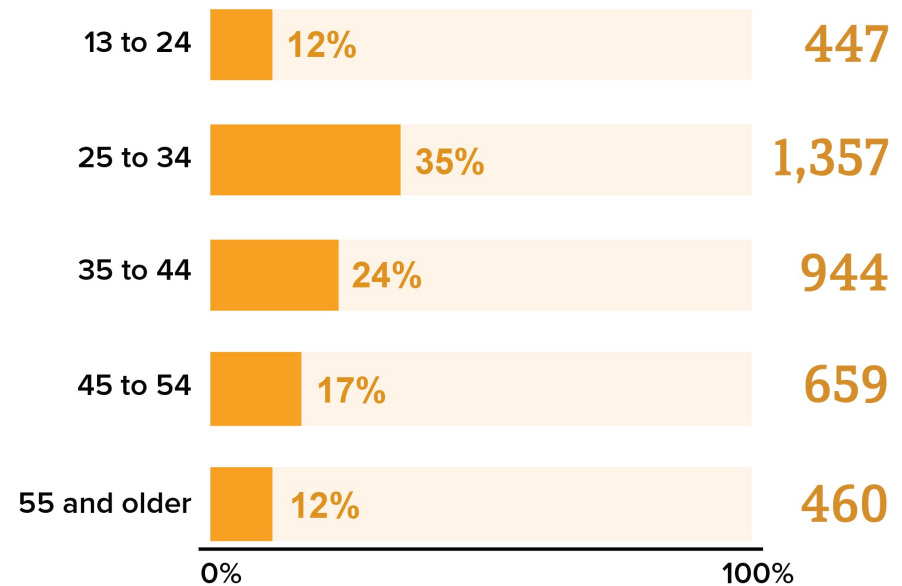
† *Black* refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.

‡ Hispanic/Latino people can be of any race.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

New HIV Diagnoses Among People Who Inject Drugs in the US and Dependent Areas by Age, 2018*

People aged 13 to 34 made up nearly half of all new HIV diagnoses among people who inject drugs.



The numbers have been statistically adjusted to account for missing transmission categories. Values may not equal the total number of PWID who received an HIV diagnosis in 2018.

* Includes infections attributed to male-to-male sexual contact *and* injection drug use (men who reported both risk factors).

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

Syringe Sharing Among People Who Inject Drugs in 23 US Cities, 2018


Sharing needles, syringes, or other drug injection equipment puts people who inject drugs (PWID) at high risk for HIV and other infections.

 32% of PWID shared syringes


Syringe sharing is more common among young people.

 48% of people aged 18 to 24 shared syringes

 44% of people aged 25 to 29 shared syringes

 39% of people aged 30 to 39 shared syringes

 30% of people aged 40 to 49 shared syringes

 23% of people aged 50 and older shared syringes

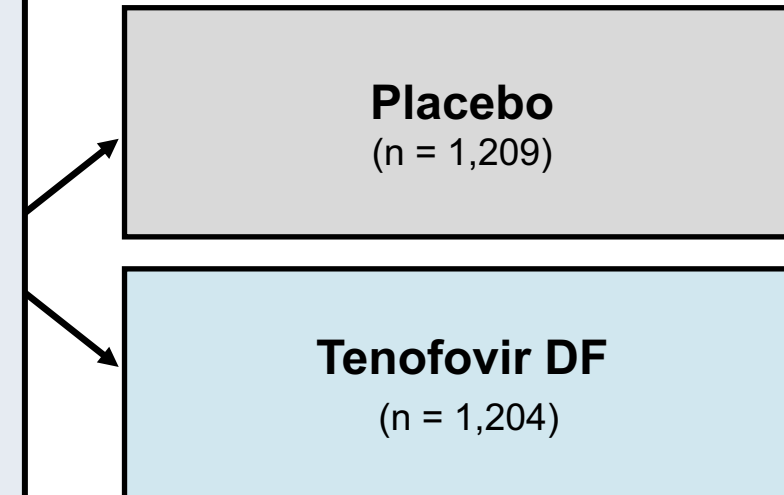
Source: CDC. HIV infection risk, prevention, and testing behaviors among persons who inject drugs—National HIV Behavioral Surveillance: Injection drug use – 23 U.S. Cities, 2018. *HIV Surveillance Special Report 2020*; 24.

Evidence Supporting the Use of PrEP in PWID and CDC Recommendations

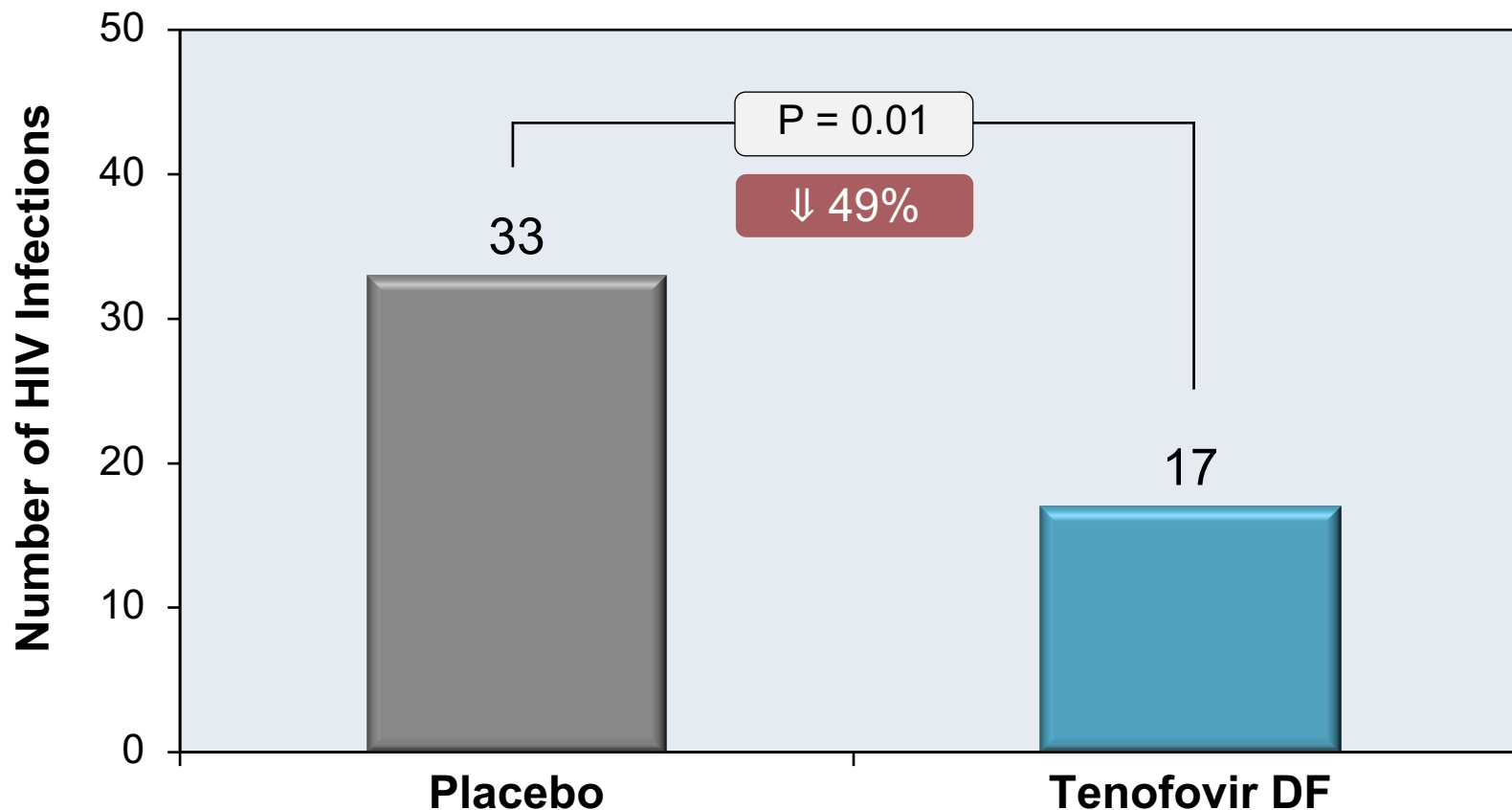
PrEP with Tenofovir DF for Persons who Inject Drugs Bangkok Tenofovir Study: Background

Study Design: Bangkok Tenofovir Study

- **Background:** Randomized, phase 3, double-blind, placebo-controlled trial conducted in Bangkok, Thailand that examined efficacy and safety of tenofovir DF as preexposure prophylaxis in persons who inject drugs
- **Inclusion Criteria** (2,413 enrolled)
 - 20-60 years of age
 - HIV-1-negative
 - Reported injecting drugs in prior year
 - All subjects received risk-reduction counseling
 - All subjects received bleach and condoms
 - Excluded if HBsAg+
 - Excluded if pregnant or breastfeeding
- **Treatment Arms:**
 - Placebo: 1 pill daily
 - Tenofovir DF: 1 pill daily



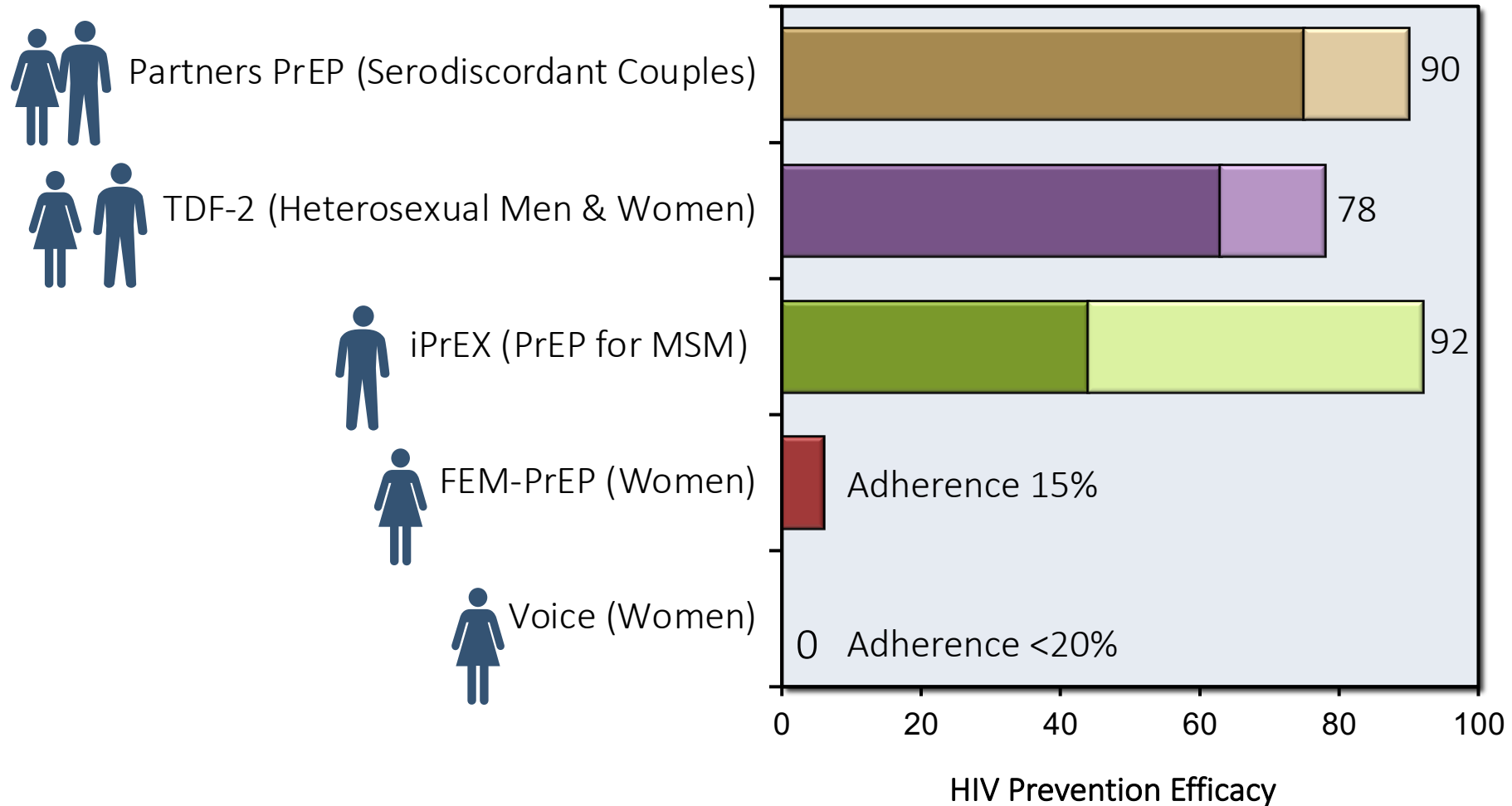
PrEP with Tenofovir DF for Persons who Inject Drugs Bangkok Tenofovir Study: Results (Modified Intent-to-Treat)



This analysis does not include 2 additional HIV infections in placebo group that were identified at enrollment
Follow-up time: mean 4.0 years (SD 2.1; max 6.9 years)

Estimated Protection in Adherent Participants

All Participants (Dark Bar) vs Adherent Participants (Light Bar)



DISCOVER Trial: TAF/FTC for PrEP

- Design: Multicenter non-inferiority RCT of TDF/FTC vs TAF/FTC
- Population: 5,387 MSM and TGW at high risk of HIV
- Primary Endpoint: HIV incidence
- Results
 - TAF/FTC non-inferior to TDF/FTC
 - Bone: Less decrease in BMD at hip and spine
 - Renal: Less renal injury

Only MSM & TGW in the study population; **cannot** extrapolate to persons having receptive vaginal sex or PWID

Alternative to daily PrEP: IM Cabotegravir

- Design: Multicenter, double blind, randomized control trial
 - Injectable cabotegravir q8w + placebo VS daily TDF/FTC + placebo injection
- Population
 - HPTN 083: 4570 MSM and TGW from 43 sites across 3 continents
 - HPTN 084: 3224 cisgender women ages 18-45 in sub-Saharan Africa
- Primary Endpoint: HIV infection
- Result
 - HPTN 083: IM Cabotegravir non-inferior to TDF/FTC
 - HTPN 084: IM Cabotegravir is superior to TDF/FTC for PrEP

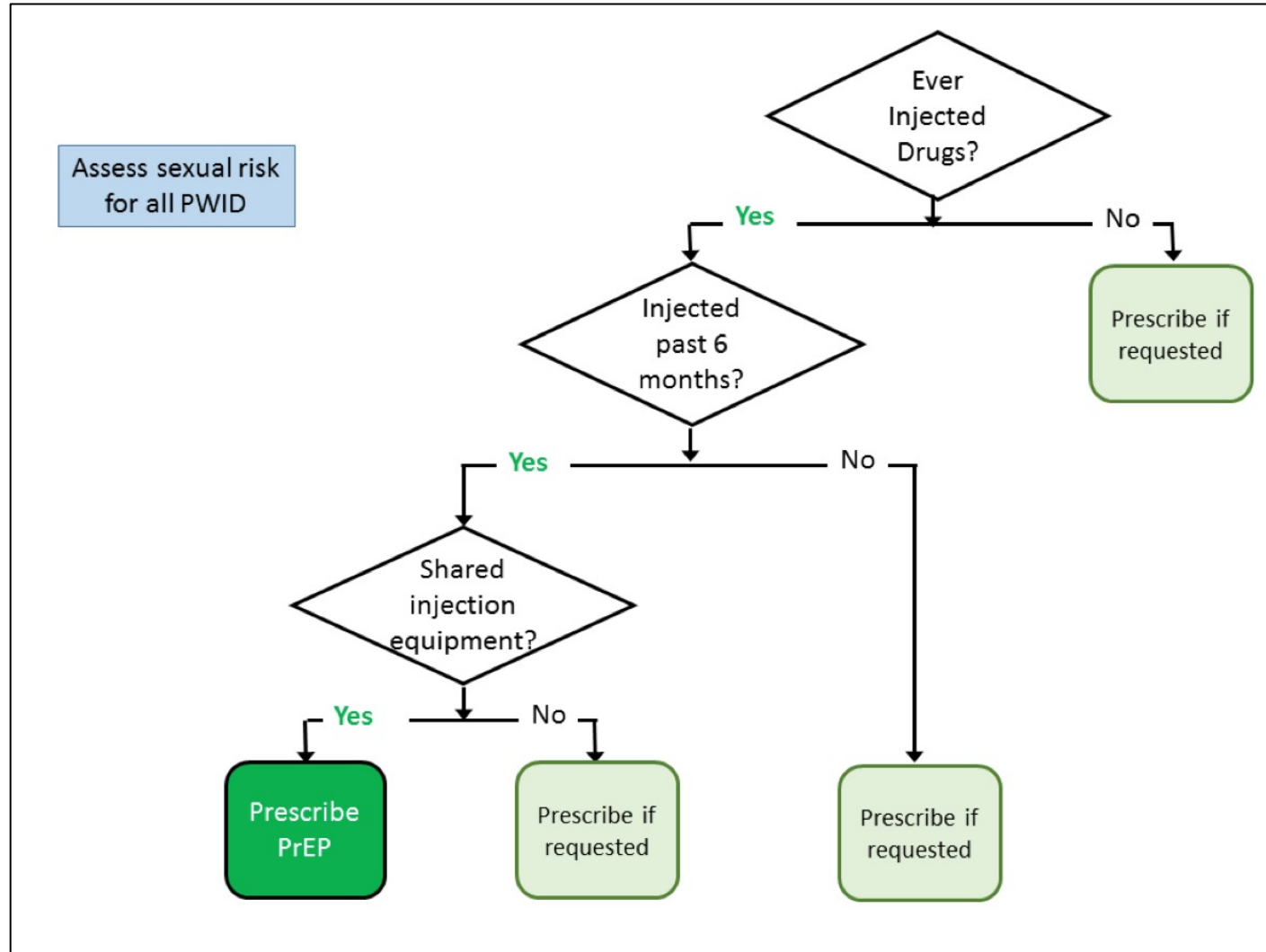
CDC Indications for PrEP

	HIV+ Partner	Recent Bacterial STI	Multiple Sex Partners	Sex Without Condoms	Exchange Sex	Sharing injection equipment
MSM	✓	✓	✓	✓	✓	
Heterosexual M/W	✓	✓	✓	✓	✓	
PWID*	✓	✓	✓	✓	✓	✓

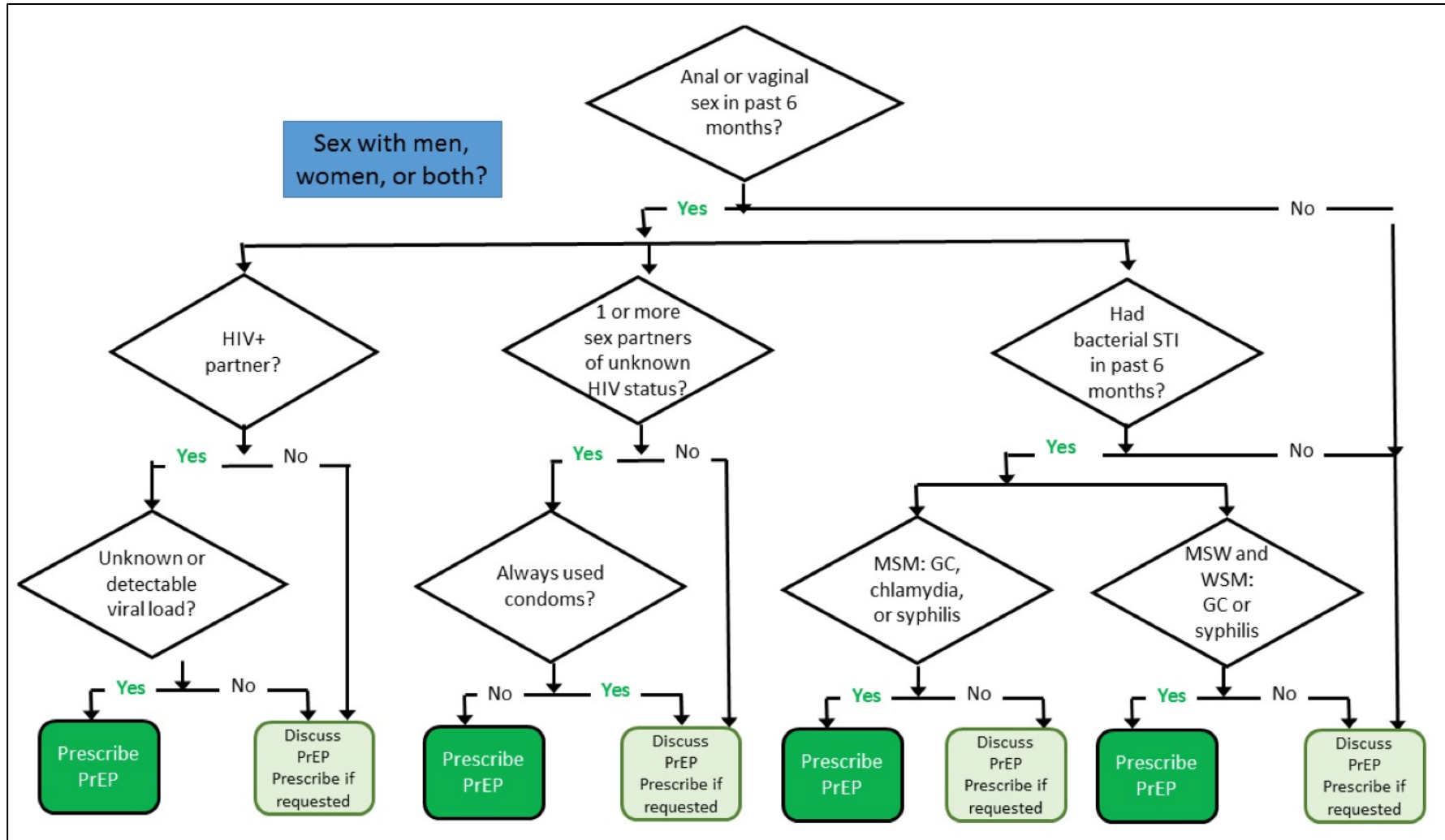
*PWID = person with injection drug use

Anyone at risk for HIV

CDC Indications for PrEP: Injection Drug Use



CDC Indications for PrEP: Sex



Which medication should I prescribe for daily PrEP?

TDF/FTC (Truvada)

FDA approval: 2012



19 mm



EFFECTIVENESS

- ✓ for multiple populations

SAFETY

- Small ↓ in eGFR and BMD

COST

- \$1,845/month in 2019
- Generic in 2020



EFFECTIVENESS*

MSM & TRANS WOMEN
HETEROSEXUALS
PWID

SAFETY / 48 WKS

eGFR (mL/min)
HIP BMD
LDL (mg/dL)
BODY WEIGHT (kg)



12.5 mm

TAF/FTC (Descovy)

FDA approval: 2019



EFFECTIVENESS

- ✓ for MSM and transwomen
- ? for other populations

SAFETY

- Small ↑ in LDL and weight

COST

- \$1,845/month in 2019



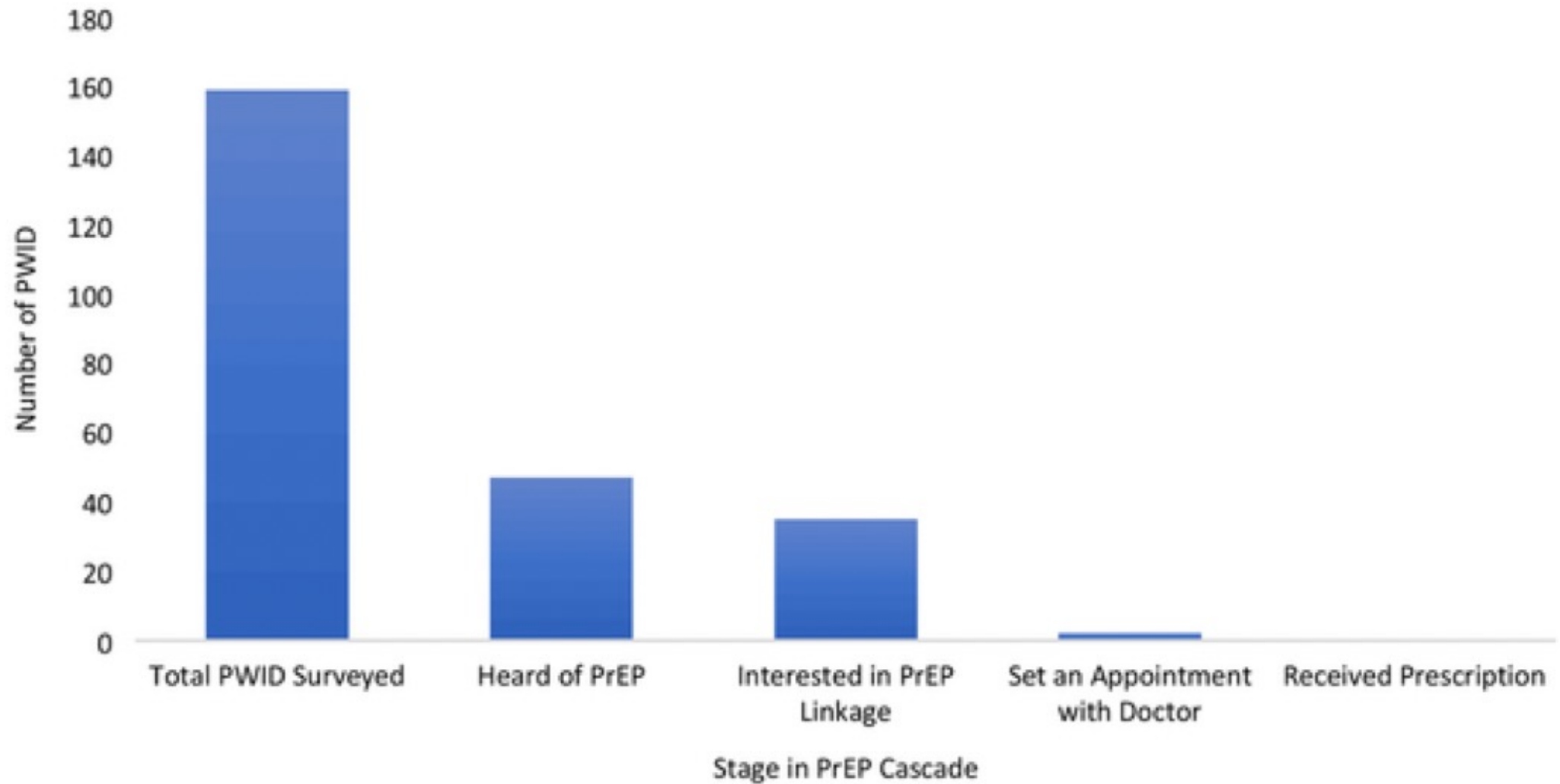
*No data available for trans men. Sources: [fda.gov/media/129607/download](https://www.fda.gov/media/129607/download); [fda.gov/media/129609/download](https://www.fda.gov/media/129609/download); [cdc.gov/hiv/risk/estimates/preventionstrategies.html](https://www.cdc.gov/hiv/risk/estimates/preventionstrategies.html) Created by: @JuliaLMarcus

Challenges in the Implementation of PrEP for PWID

PrEP has
been
underutilized
for PWID

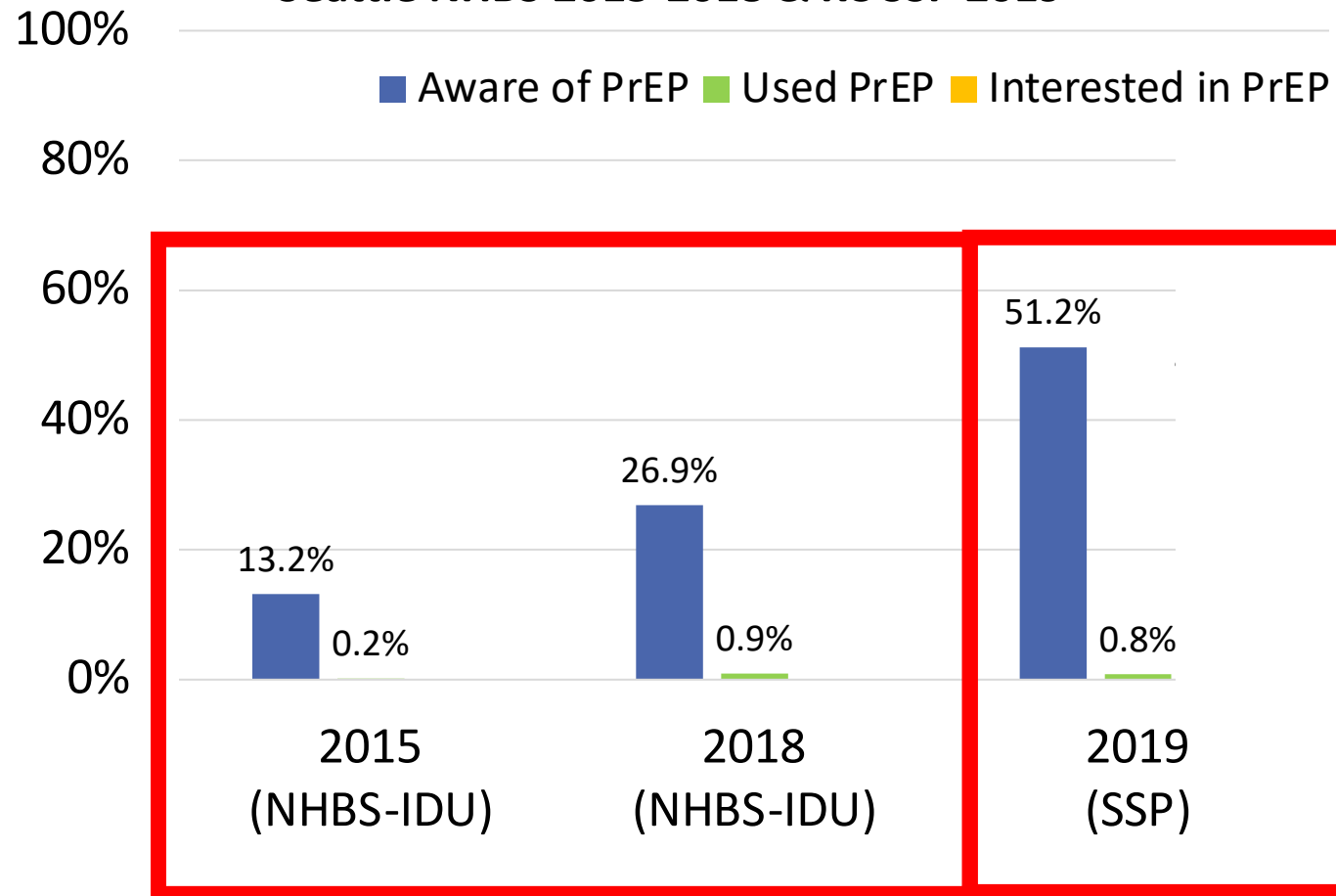
- Among 265 HIV-uninfected PWID in Baltimore, only 2 (0.75%) were currently taking PrEP despite 43% being eligible for PrEP based on injection behavior.
- 2015 NHBS data in Philadelphia showed that only 2.6% of 612 HIV-negative PWID surveyed had received a prescription for PrEP.
- A survey of PWID in San Francisco found that only 3.0% of PWID reported taking PrEP

Figure 2. PrEP Cascade among PWID accessing syringe services in Miami, FL in 2019 (Jo et al, 2020)



PrEP

**PrEP Awareness, Use, and Interest among PWID,
Seattle NHBS 2015-2018 & KC SSP 2019**

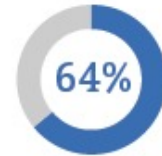


Awareness of PrEP and Risk Perception Among PWID

- In a systematic review of the PrEP care cascade in PWID:
 - PrEP awareness ranged from >1% to 57%
 - Risk perception range from 1.1% to 66%
 - Among the studies reviewed, factors associated with willingness to use PrEP were varied:
 - Perception of risk for HIV
 - Appropriate support services (e.g., social support, support from clinicians)
 - Female gender
 - Identifying as bisexual
 - Homelessness
 - Other medical comorbidities
 - Being PrEP eligible (e.g., risk factors for HIV)

Selected Characteristics Among PWID With HIV in 23 US Cities, 2018

Social and economic factors may limit access to HIV treatment services among PWID with HIV.



reported being homeless



reported being incarcerated

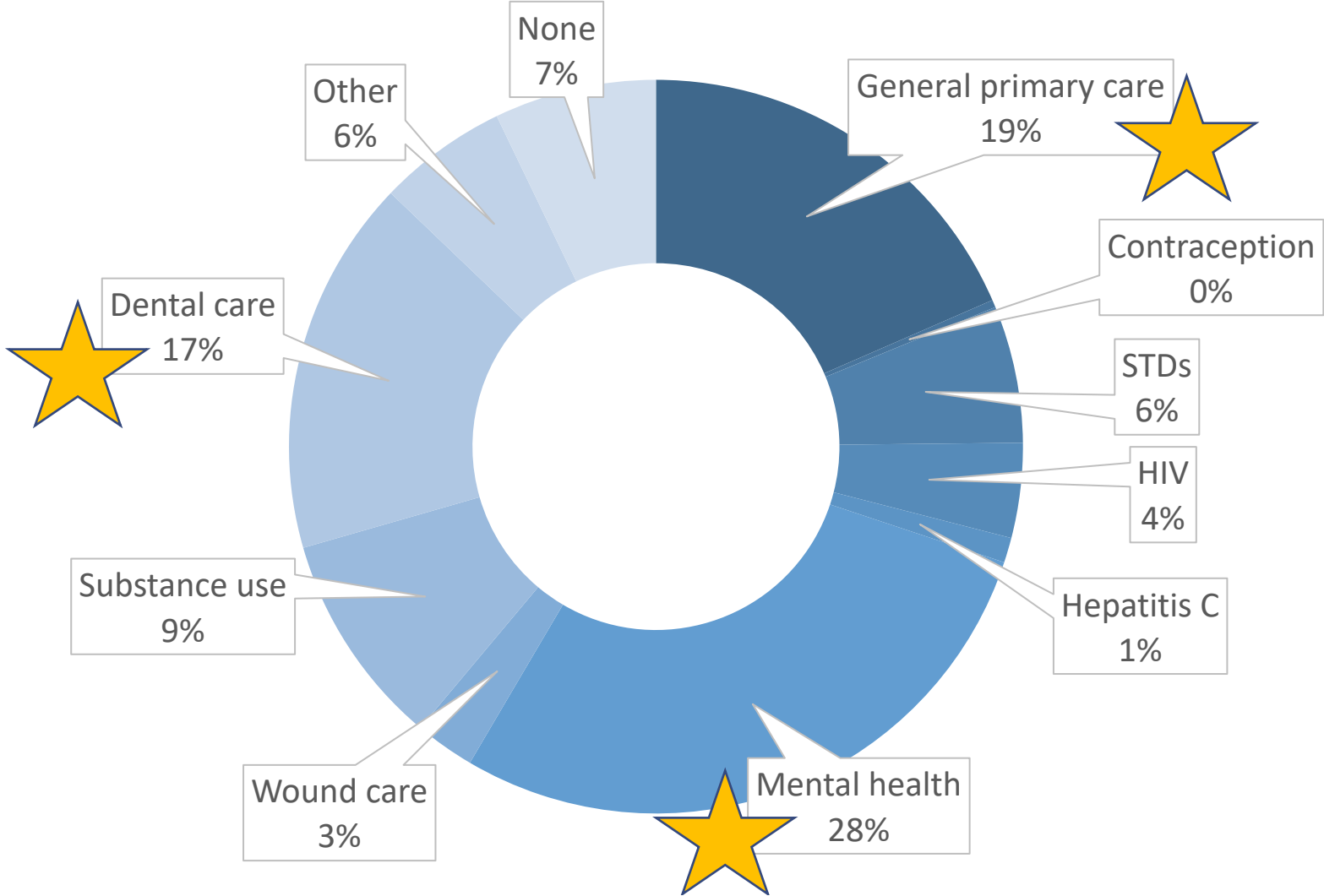


reported having no health insurance

Source: CDC. HIV infection risk, prevention, and testing behaviors among persons who inject drugs—National HIV Behavioral Surveillance: Injection drug use – 23 U.S. Cities, 2018. *HIV Surveillance Special Report 2020*; 24.

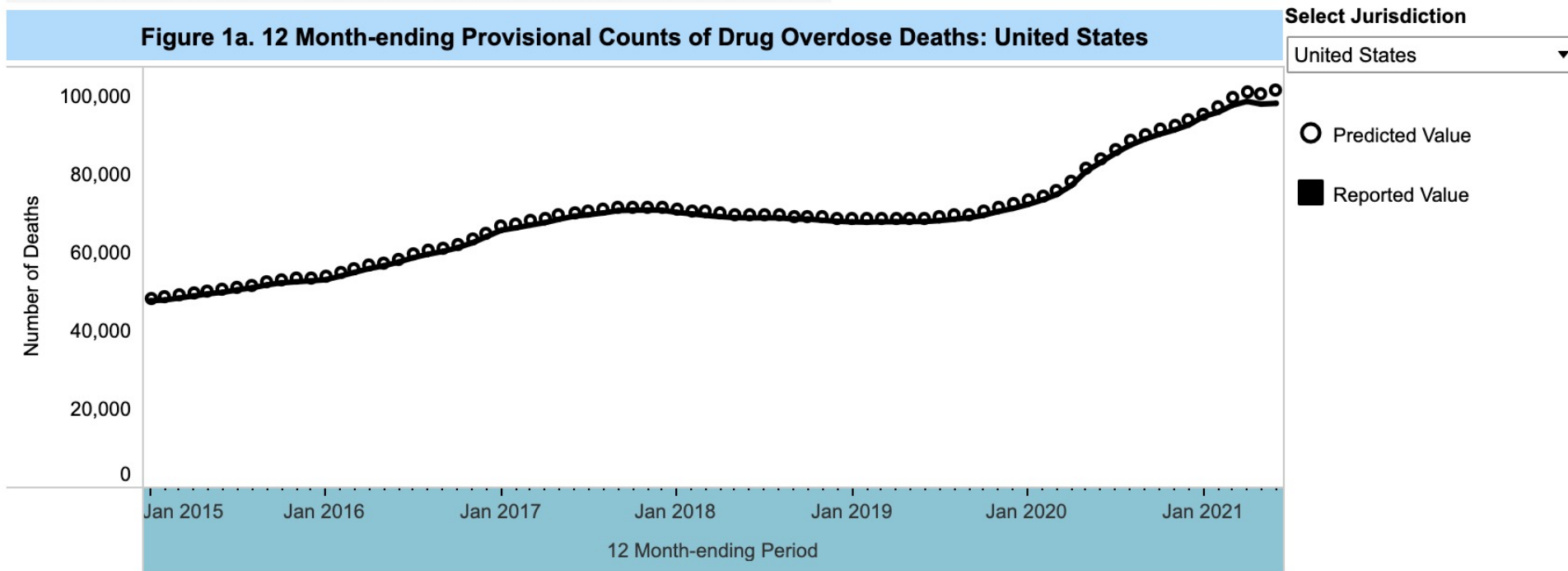
What is your most important medical concern right now?

Among women who exchange sex, Seattle NHBS 2016

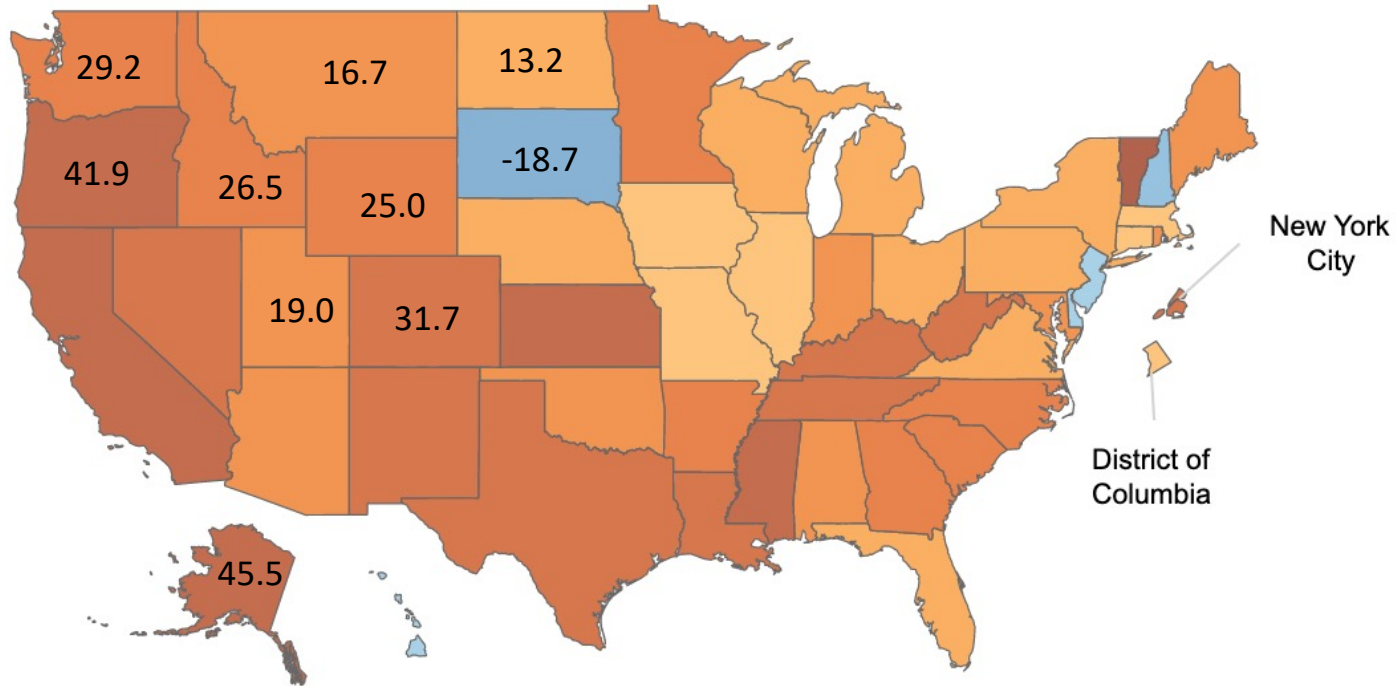


12 Month-ending Provisional Number of Drug Overdose Deaths

Based on data available for analysis on: **1/2/2022**



**Figure 1b. Percent Change in Predicted 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction:
June 2020 to June 2021**



Select predicted or reported number of deaths

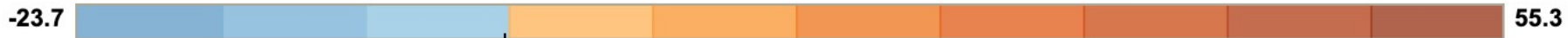
- Predicted
- Reported

Percent Change for United States

20.6



Legend for Percent Change in Drug Overdose Deaths Between 12-Month Ending Periods



Decreased HIV Testing During the COVID-19 Pandemic

Qualitative and quantitative data from syringe service programs (SSPs) indicate that HIV (and HCV) testing was put on hold or significantly reduced at the beginning of the COVID-19 pandemic.

Unpublished data from a survey of SSPs indicate that HIV testing remains below the pre-COVID baseline for ~50% of SSPs

Future Directions for PrEP Delivery among PWID

Improving PrEP Uptake and Sustained Use Among PWID

- There is relatively few data on concrete strategies to improve PrEP uptake and sustained use among PWID
- Many novel strategies, such as “home PrEP,” “tele-PrEP,” community pharmacy-based PrEP, and “on-demand PrEP” many not be well suited towards PWID.

Qualitative Assessment of PrEP Services in King County, Washington (2019)

- 18 interview with service providers and 3 focus groups with PWID (n=27):
 - Overall support for PrEP for PWID
 - Should be on the menu of HIV prevention options, but not at the expense of other interventions
 - More education is needed among PWID and providers
 - Three potential models:
 1. **Drug user health center** – fixed site addressing a rang of services on a walk-in basis
 2. **Mobile outreach** – outreach worker-led program engaging with clients in the field
 3. **Add-on to existing service provider** (e.g., SSPs)

Integrating PrEP into Syringe Services for Women

- Demonstration project in Philadelphia aiming to integrate PrEP into existing SSP services for women who inject drugs (WWID).
- WWID ≥ 18 years of age, who were HIV negative at baseline and not pregnant or planning to become pregnant, were educated about and offered 24 weeks of daily PrEP.
- Participants completed surveys and clinical assessment at baseline and weeks 1, 3, 12, and 24.
 - TDF drug levels in urine were obtained at week 12 and 24 to assess adherence

Results

- 95 women were enrolled
 - 63.4% currently homeless
 - 39.6% visited SSP a “few times a week,” 16.5% visited “daily”
 - 46.2% reported sharing syringes in the past 6 months
 - 71.6% reported transactional sex, with 78.9% reporting inconsistent condom use
 - 54.3% reported their self-perceived risk of HIV to be extremely or very low
 - 45.7% reported their self-perceived risk of HIV to be somewhat/very/extremely high

Results

- Of the 95 women enrolled, 69 received a prescription of PrEP in week 1 and 43 were maintained on PrEP by week 12.
- 5 women who initially did not receive a PrEP prescription in week 1 initiated PrEP by week 12.
- Of the 48 WWID on PrEP at week 12, 23 persistent on PrEP by week 24.

Adherence to PrEP

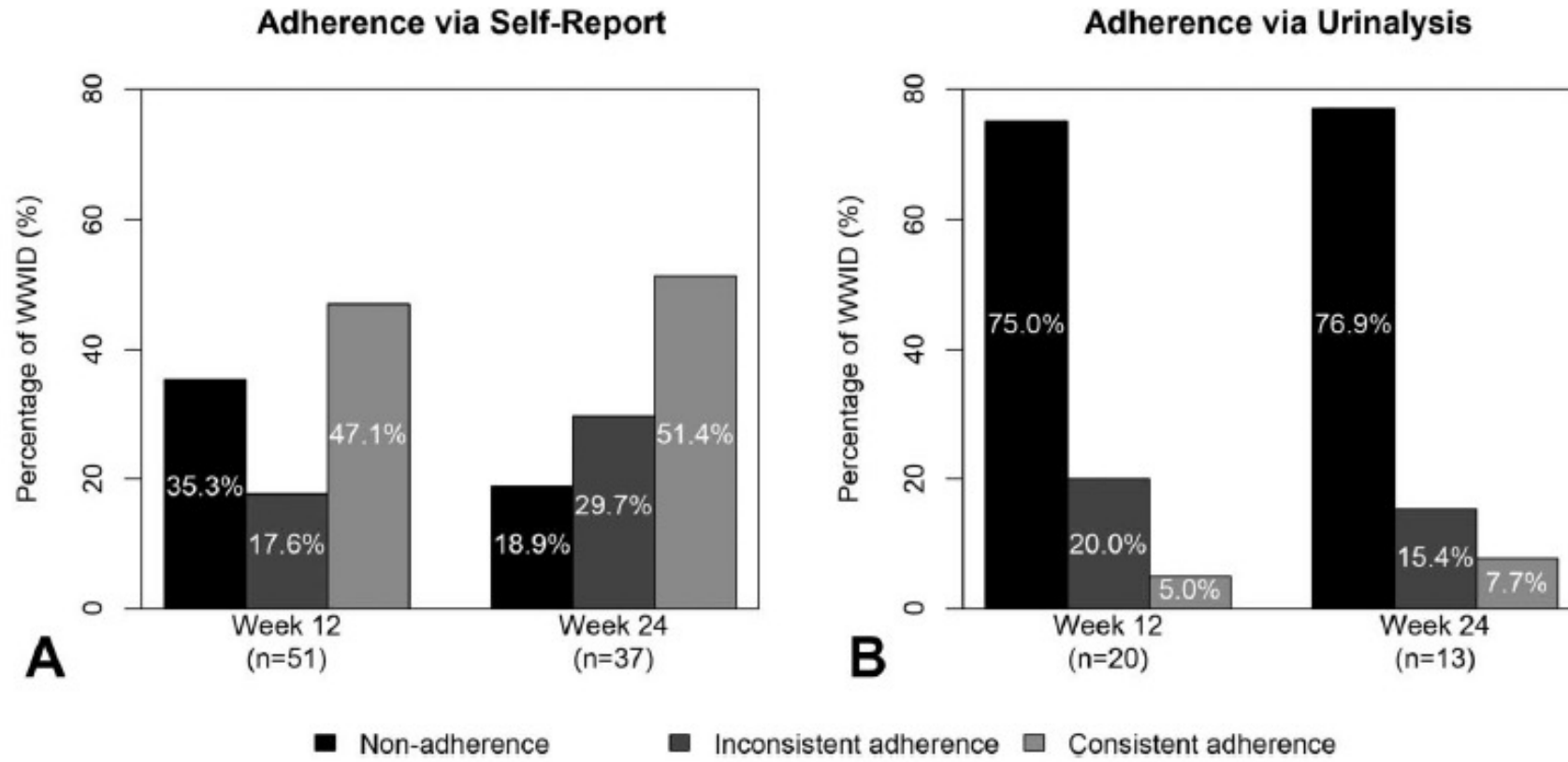


TABLE 3. Correlates of PrEP Uptake and Retention in Care Among Women Who Inject Drugs (n = 95) Enrolled in a PrEP Demonstration Project in Philadelphia

	A. PrEP Uptake		B. Retention in Care	
	OR (95% CI)	aOR (95% CI)*	OR (95% CI)	aOR (95% CI)†
Age, yr	1.00 (0.95 to 1.05)		1.07 (1.02 to 1.13)	
Race/ethnicity				
White, non-Hispanic	Ref		Ref	
Black, non-Hispanic	0.89 (0.28 to 2.82)		0.88 (0.27 to 2.73)	
Hispanic/Latino	0.78 (0.21 to 2.84)		1.59 (0.44 to 6.01)	
Mixed race, non-Hispanic	2.68 (0.22 to 33.6)		1.32 (0.15 to 11.6)	
Education				
Less than high school	Ref		Ref	
High school grad	0.93 (0.35 to 2.45)		0.45 (0.16 to 1.17)	
Some college or higher	1.30 (0.45 to 3.72)		0.67 (0.24 to 1.85)	
Currently homeless	1.01 (0.42 to 2.42)		1.29 (0.55 to 3.07)	
Current housing				
Own home	1.20 (0.19 to 7.62)		1.29 (0.22 to 7.78)	
Staying with family/friends	0.74 (0.26 to 2.07)		0.73 (0.25 to 2.03)	
Single room occupancy	1.14 (0.28 to 4.67)		1.08 (0.27 to 4.18)	
Living in shelter/treatment facility	1.36 (0.38 to 4.98)		1.73 (0.51 to 6.16)	
Living on street	Ref		Ref	
Frequency of SSP access	1.56 (1.16 to 2.09)	1.85 (1.24 to 2.77)	1.44 (1.08 to 2.06)	1.46 (1.04 to 2.24)
Sharing syringes	0.75 (0.32 to 1.73)		0.50 (0.21 to 1.13)	
No. sexual partners	1.00 (0.99 to 1.01)		1.00 (0.99 to 1.00)	
Inconsistent condom use	2.79 (1.03 to 7.53)	3.38 (1.07 to 10.7)	0.66 (0.24 to 1.74)	
Transactional sex	0.74 (0.29 to 1.85)		0.80 (0.33 to 1.97)	
Baseline STI diagnosis	0.96 (0.32 to 2.84)		0.64 (0.20 to 1.85)	
Sexual assault (n = 67)‡	5.03 (1.14 to 22.2)	5.89 (1.02 to 33.9)	1.52 (0.47 to 4.89)	
Self-perceived HIV risk				
Extremely/very unlikely	Ref		Ref	
Somewhat/very/extremely likely	1.29 (0.56 to 3.02)		0.78 (0.34 to 1.76)	

*Model was adjusted for follow-up period, age, race/ethnicity, and current housing.

†Model was adjusted for age, race/ethnicity, and current housing.

‡Model was restricted to women who received the question on sexual assault at baseline.

Coupling PrEP with HCV Treatment for PWUD with OUD – ANCHOR Study

- Study evaluating a community-based care model, collocating HCV treatment, MOUD, and PrEP in Washington DC and Baltimore.
- Individuals were enrolled if they were HCV RNA+ and had opioid misuse within the past year.
 - Based on site characteristics, all participants receiving care at the Baltimore site were on MOUD. Participants in DC were offered MOUD.
- Patients meeting inclusion criteria (no decompensated liver disease, contraindications to DAA, pregnancy/breastfeeding) were started on DAA therapy for HCV at day 0.
- HIV negative participants were screened for interest in and knowledge of PrEP and were offered PrEP based on 2014 CDC guidelines.
 - Interest in PrEP was assessed at each study visit during a 6-month window (week 0 to 24) and participants could start at any time.
 - Participants who initiated PrEP were followed through week 48.

Coupling PrEP with HCV Treatment for PWUD with OUD – Results

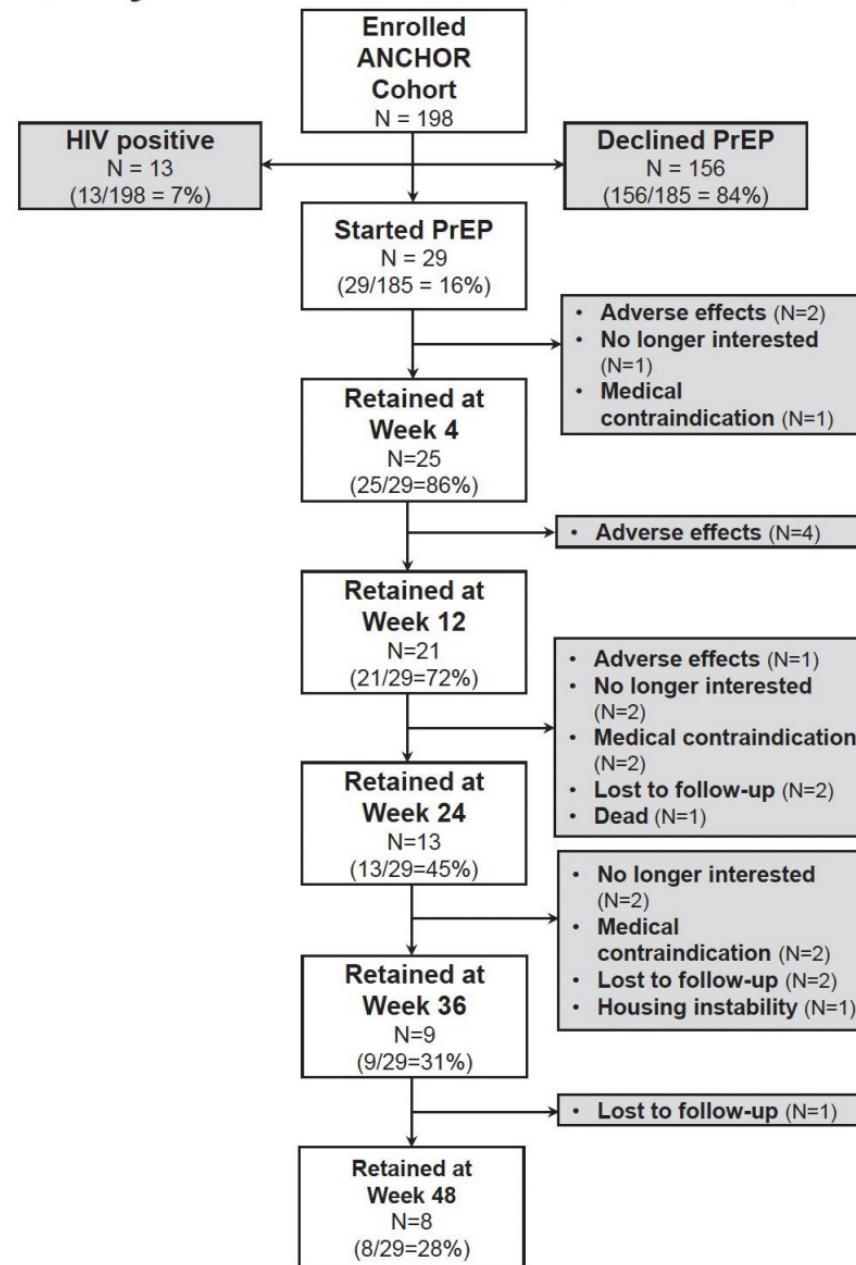
- 195 participants were enrolled, 185 (93%) of whom were HIV negative.
- 62.7% met 2014 CDC PrEP eligibility criteria
 - 44.3% met IDU criteria only
 - 4.9% met sex criteria only
 - 13.5% met both criteria
- Clinicians recommended PrEP to 94 (50.8%) individuals
- 29 (15.7% of HIV- cohort) participants initiated PrEP

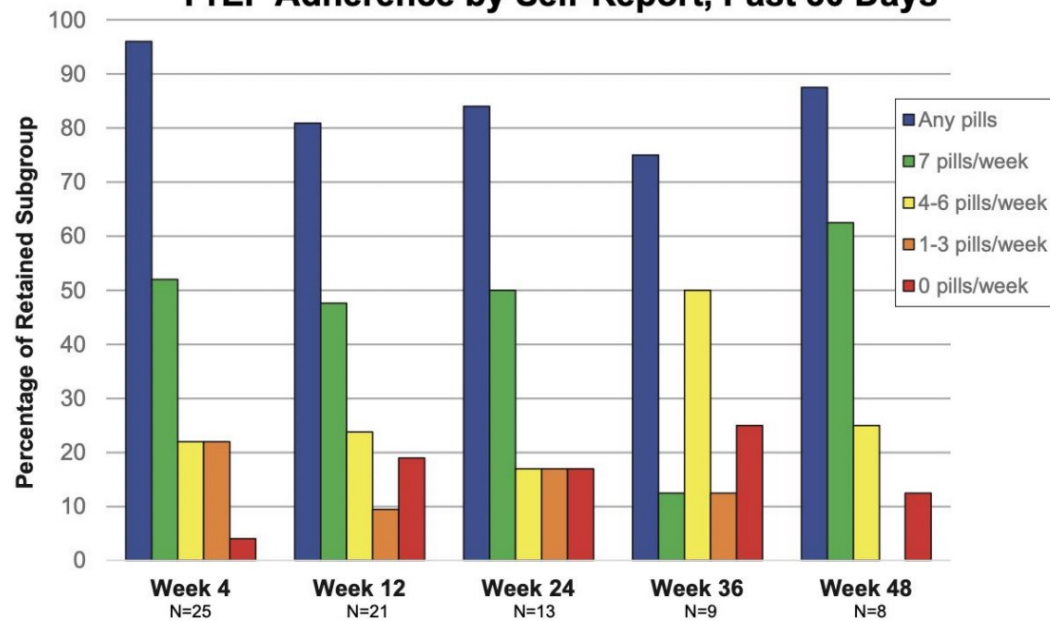
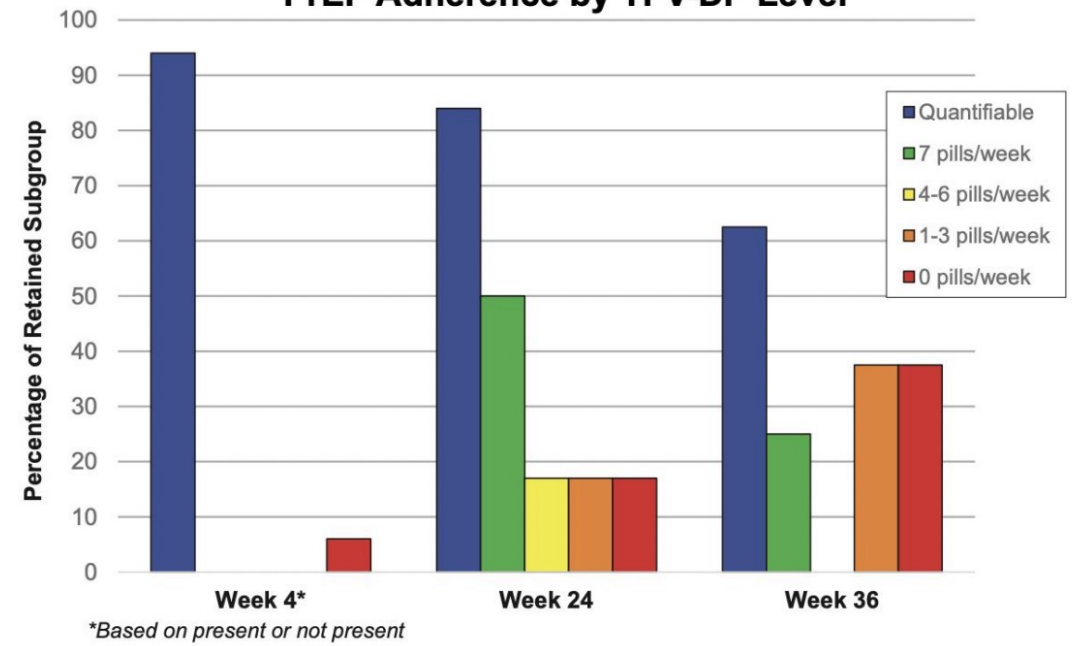
Table 1. Baseline Population Characteristics				
Characteristic	HIV-Negative N=185	PrEP N=29	No PrEP N=156	P-value
<i>Demographics</i>				
Median age (IQR), years	57 (52, 61)	54 (52, 60)	58 (52, 61)	0.20
Male, N (%)	129 (69.7)	21 (72.4)	108 (69.2)	0.83
Black race	155 (83.8)	26 (89.7)	129 (82.7)	0.42
Heterosexual	172 (93.0)	27 (93.1)	145 (92.9)	1
<i>Baseline Epidemiology</i>				
Unstably housed, N (%)	101 (54.6)	17 (58.6)	84 (53.8)	0.69
Drug use daily or > frequency	111 (60.0)	21 (72.4)	93 (59.6)	0.22
Receptive needle sharing, past year	24 (13.0)	7 (24.1)	17 (10.9)	0.07
Receptive IDU equipment sharing, past year	54 (29.2)	8 (27.6)	46 (29.5)	1
>1 sex partner, past year	33 (17.8)	8 (27.6)	25 (16.0)	0.18
Condomless vaginal sex, past year	72 (38.9)	12 (41.4)	60 (38.5)	0.84
Condomless anal sex, past year	11 (5.9)	2 (6.9)	9 (5.8)	0.68
Transactional sex, past year	10 (5.4)	2 (6.9)	8 (5.1)	0.66
<i>2014 CDC Eligibility</i>				
Met IDU criteria only, N (%)	82 (44.3)	10 (34.5)	72 (46.2)	0.63
Met sex criteria only	9 (4.9)	2 (6.9)	7 (4.5)	0.31
Met both criteria	25 (13.5)	9 (31.0)	16 (10.3)	0.006

Coupling PrEP with HCV Treatment for PWUD with OUD – Results

- Median treatment duration for those initiating PrEP was 104 days (IQR 28, 276).
- 8 participants were retained on PrEP through the 48-week timepoint.
- Most common reason for discontinuation was side effects (n/v most frequent)

Study Enrollment and PrEP Continuum



A**PrEP Adherence by Self-Report, Past 30 Days****B****PrEP Adherence by TFV-DP Level**

SHE Clinic: Co-located, low-barrier services

- SHE Clinic provides low-barrier walk-in medical services to women living unhoused, many of whom inject drugs, in north Seattle
 - Co-located within the Aurora Commons, a day drop-in center for unhoused individuals

Table 3: Utilization of HIV harm-reduction services among 76 women accessing day-shelter services in north Seattle, by care at SHE Clinic

Characteristics	SHE Clinic patients (n=41)	SHE Clinic non-adopters (n=35)	p-value
Recent STI screening	34 (83)	22 (63)	0.03
Recent STI treatment	13 (32)	3 (9)	0.06
Opioid replacement*	21/36 (58)	3/22 (14)	0.001
PrEP prescription*	18/37 (49)	0/22 (0)	<0.001

*calculated for those eligible for intervention (opiate dependent or HIV negative)

Aurora Clinic: Approach to PrEP

1. Discuss risk factors for HIV – (IDU, sex, both)
2. Ask about prior HIV testing
3. Assess awareness of and interest in PrEP
4. Screen for s/sx of acute HIV as well as indications for PEP
5. Rapid HIV test (INSTI)
6. Blood draw for 4th generation HIV ag/ab, creatinine, HBsAg, HCV, STIs
7. If rapid HIV negative and no c/f acute HIV, prescribe 1 mo TDF/FTC
8. Discuss other harm reduction strategies including MOUD, condoms, SSPs
9. F/u on 4th gen HIV ag/ab → if positive contact patient to start 3rd agent

Stuck in the window with you

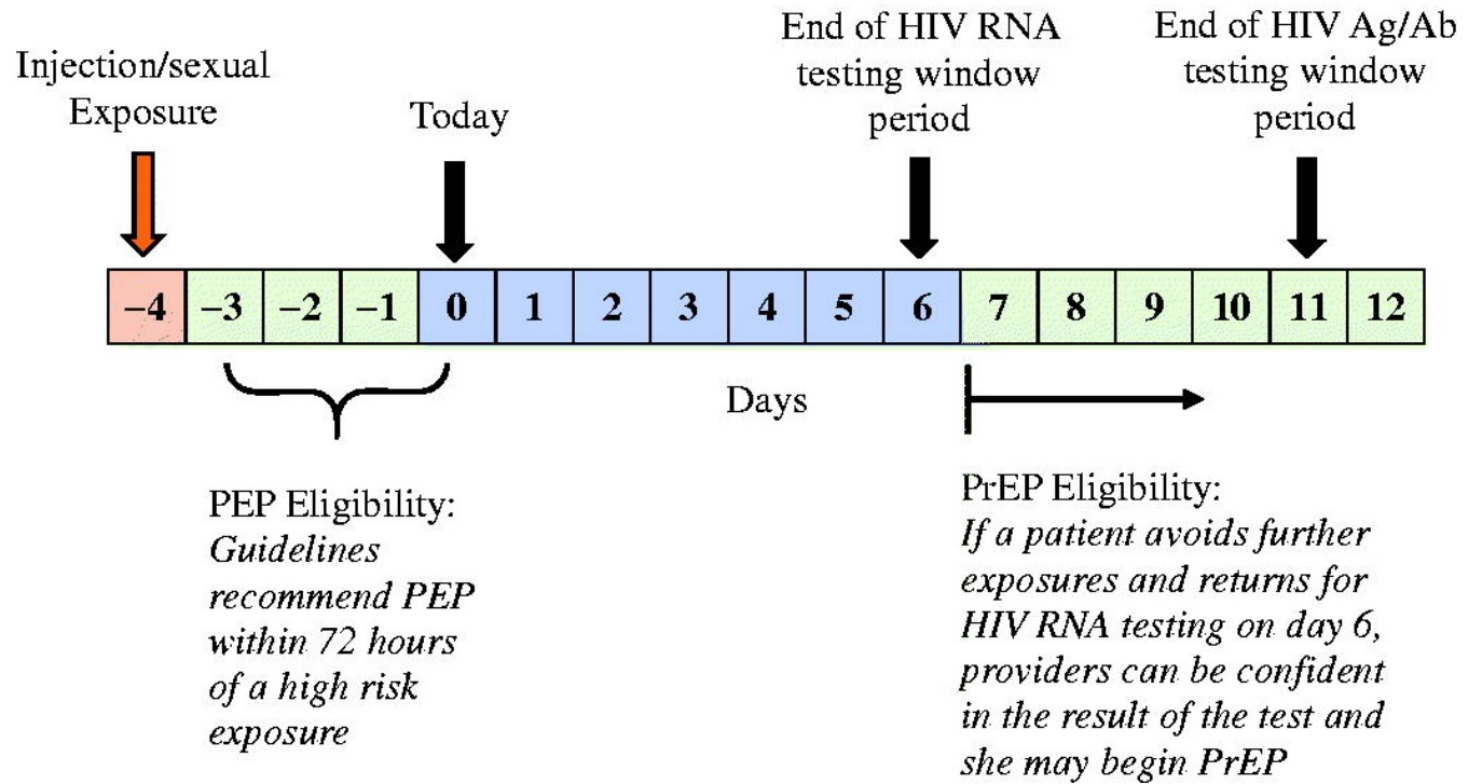


Figure 1. The HIV exposure prophylaxis eligibility and HIV testing window periods.

What can we learn from HIV treatment adherence strategies among PWID?

- Bazzi et.al. conducted a systematic review of HIV treatment adherence research in PWID, which included 20 studies.
- Factors enabling ART adherence included:
 - Substance use treatment, including MOUD
 - Self-efficacy, empowerment and social support
 - Stable housing
 - Health insurance
 - Trust in providers and good patient-provider relationships
 - Accessibility of health care services
 - Directly administered ART

Looking forward

- Additional work is needed to integrate PrEP into low-barrier services for PWID, including drug treatment programs, SSPs, other community-based organizations, and primary care.
- More research is needed to identify successful strategies to improve both uptake AND sustained use of PrEP among PWID.
- Cabotegravir has the potential to improve sustained use of PrEP, particularly among PWID with concurrent sexual risk factors for HIV.

Conclusions

- PWID remain disproportionately affected by HIV, with several recent outbreaks of HIV within PWID communities.
- PrEP should be offered to all PWID who have shared injection equipment in the past 6 months or who have sexual risk factors.
- TDF/FTC remains the only guideline recommended medications for HIV prevention in PWID.
- Despite elevated risk for HIV, PWID experience a multitude of barriers to PrEP initiation and sustained use, including socio-structural barriers, stigma, low risk perception, and multiple competing needs.
- Integrating PrEP into other services for PWID (e.g., SSPs, drug treatment, low-barrier primary care) has the potential to improve uptake of PrEP but additional efforts are needed to identify strategies to retain PWID in PrEP services.