

PrEP Overview

HIV Pre-Exposure Prophylaxis

Sarah Rives, NP, MPH

Medical Director for HIV & PrEP - BCHD Sexual Health Clinics

Women and PrEP Symposium

12/8/21

Disclosures

- None

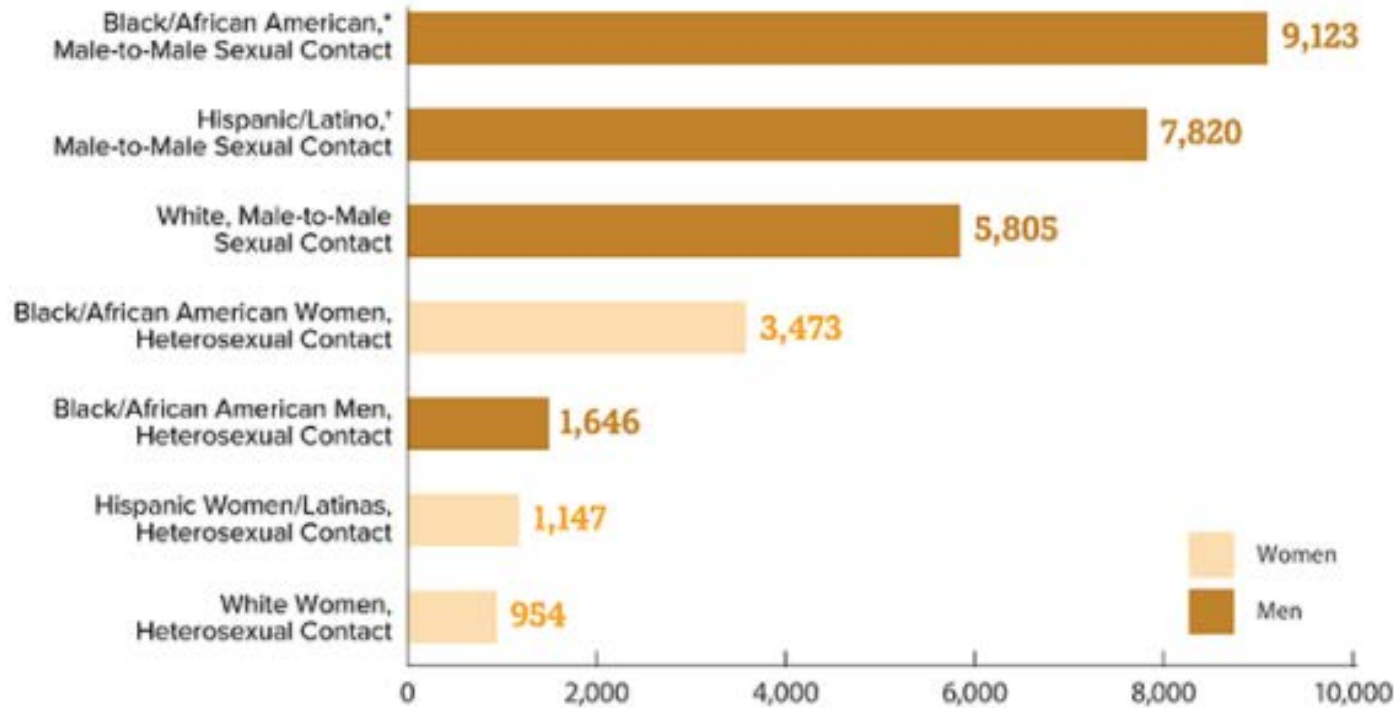
United States

1.1 million people living with HIV

37,000 new diagnoses per year

PREVENTABLE

New HIV Diagnoses in the US and Dependent Areas for the Most-Affected Subpopulations, 2019



Of the 36,801 new HIV diagnoses in the US in 2019:

Heterosexual women accounted for 16% of new diagnoses

Transgender women accounted for 2% of new diagnoses

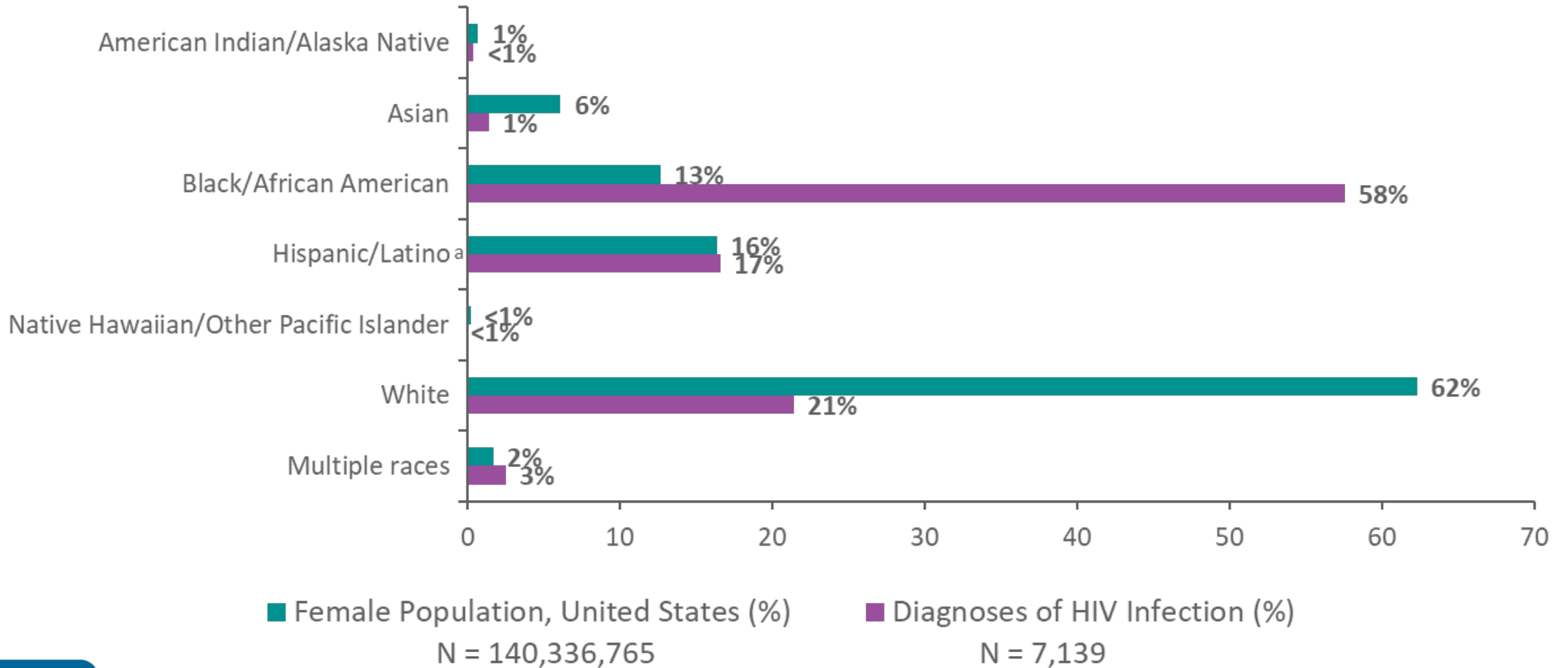
NOTE: Subpopulations representing 2% or less of all people who received an HIV diagnosis in 2019 are not represented in this chart.

* *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, 2019](#). *HIV Surveillance Report* 2021;32.

Diagnoses of HIV Infection and Population among Female Adults and Adolescents, by Race/Ethnicity, 2018—United States



Note. Data for the year 2018 are considered preliminary and based on 6 months reporting delay.

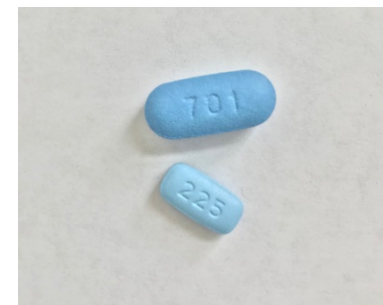
^a Hispanics/Latinos can be of any race.

<https://www.cdc.gov/hiv/library/slidesets/index.html>, accessed 12/6/21



HIV PREVENTION TOOLS

- Condoms
- Syringe exchange
- Safe blood supply
- STI diagnosis and treatment
- pMTCT
- HIV testing, linkage to care, and U=U
- PrEP
- PEP



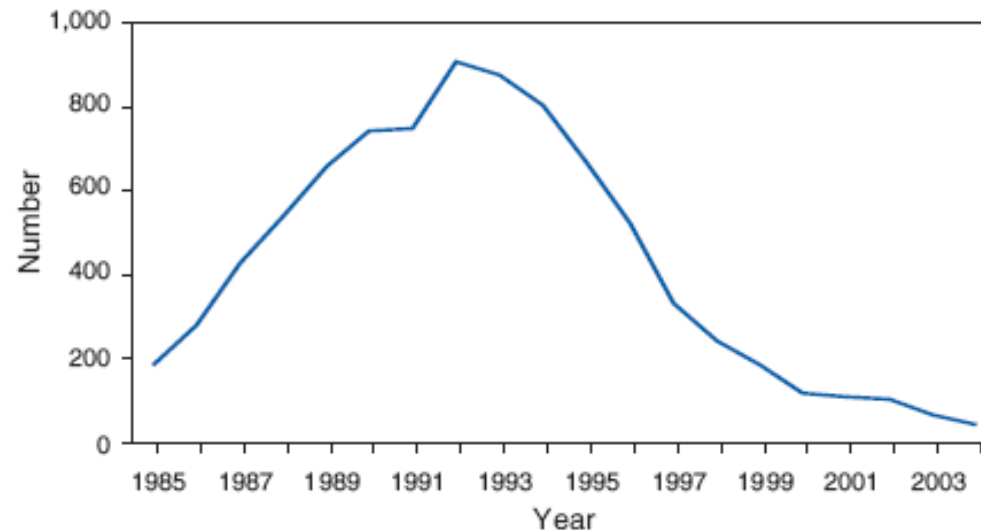
HIV Pre-Exposure Prophylaxis

Prophylaxis is a common medical intervention

- Migraines
- Malaria
- Aspirin
- Statins
- Birth control pills
- Etc...

And prophylaxis for HIV infection is not new

FIGURE. Estimated number of cases of perinatally acquired AIDS,* by year of diagnosis — United States, 1985–2004†

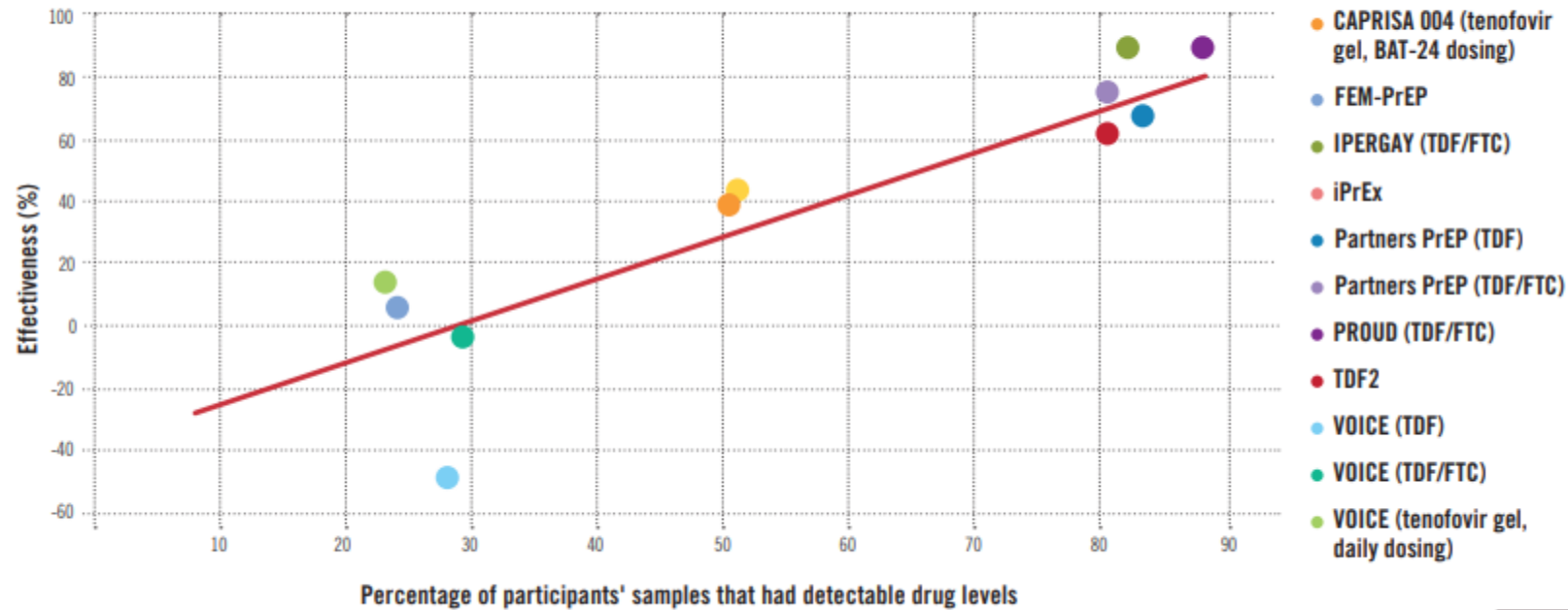


Achievements in Public Health: Reduction in Perinatal Transmission of HIV Infection – United States, 1985–2005. MMWR, June 2, 2006 55(21); 592–597.

PrEP is HIGHLY effective for HIV prevention...

PrEP works if you take it

PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



<https://www.avac.org>



How well does PrEP work for women?

- Meta-analysis of 5 RCTs of oral PrEP among women ¹
 - 3 reported evidence of effectiveness and 2 did not
 - Estimates by adherence (based on plasma drug levels)
 - **25%** adherence: **no protection** (RR 1.19 95% CI: 0.89 – 1.61)
 - **50%** adherence: **32% protective** (RR 0.68 95% CI: 0.53 – 0.88)
 - **75%** adherence: **61% protective** (RR 0.39 95% CI: 0.25 – 0.60)
- Partners PrEP study
 - Clinical trial of HIV-negative men and women in serodiscordant heterosexual relationships in Uganda and Kenya ²
 - Substudy measured plasma TDF levels among participants receiving TDF/FTC. Detectable drug level was associated with a 90% reduction in the risk of HIV acquisition

1. Hanscom et al. JAIDS 2016; 73(5):606-608

2. Baeten et al. NEJM 2012; 367(5): 399-410

History of HIV PrEP in the US

- TDF/FTC *tenofovir disoproxil fumarate + emtricitabine* (Truvada) approved by the FDA for PrEP in **2012**
- TAF/FTC *tenofovir alafenamide + emtricitabine* (Descovy) approved by the FDA for PrEP in **2019** (excluding those whose risk involves receptive vaginal sex)
- USPSTF grade A recommendation in **2019**
- Federal Government issues FAQ requiring insurers to cover PrEP without cost-sharing in July **2021**
 - <https://www.dol.gov/sites/dolgov/files/EBSA/about-ebsa/our-activities/resource-center/faqs/aca-part-47.pdf>

Recommendation Summary		
Population	Recommendation	Grade (What's This?)
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition.	A

<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis>

PrEP users in Baltimore City

PrEP (Pre-Exposure Prophylaxis)

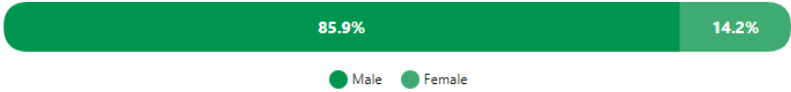
Number of PrEP users, 2019

548

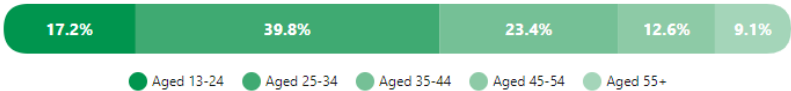
Rate of PrEP users per 100,000 population, 2019

105

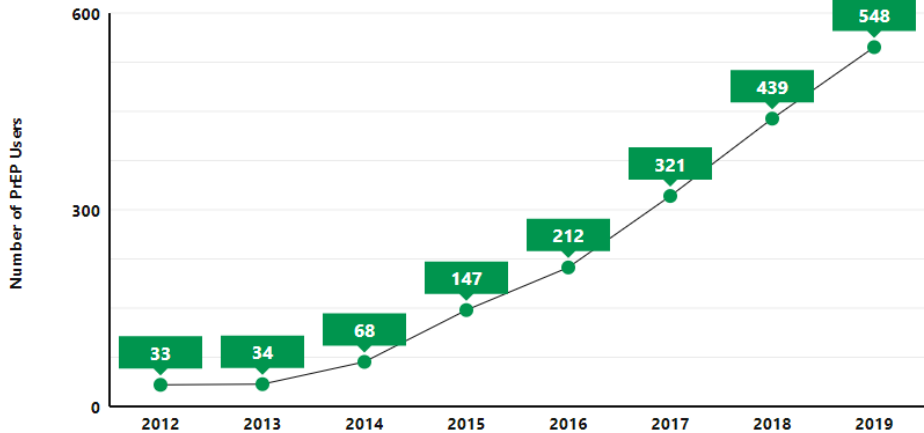
Percent of PrEP users, by Sex, 2019



Percent of PrEP users, by Age, 2019



Number of PrEP Users, 2012-2019



PrEP-to-Need Ratio (PNR) Baltimore City

The 2019 PrEP-to-Need Ratio (PNR) is the ratio of the number of PrEP users in 2019 to the number of people newly diagnosed with HIV in 2018. PNR serves as a measurement for whether PrEP use appropriately reflects the need for HIV prevention. A lower PNR indicates more unmet need.

PNR, 2019

2.37

PNR, by Sex, 2019

Male: 2.71

Female: 1.37

PNR, by Age, 2019

Aged 13-24: 2.29

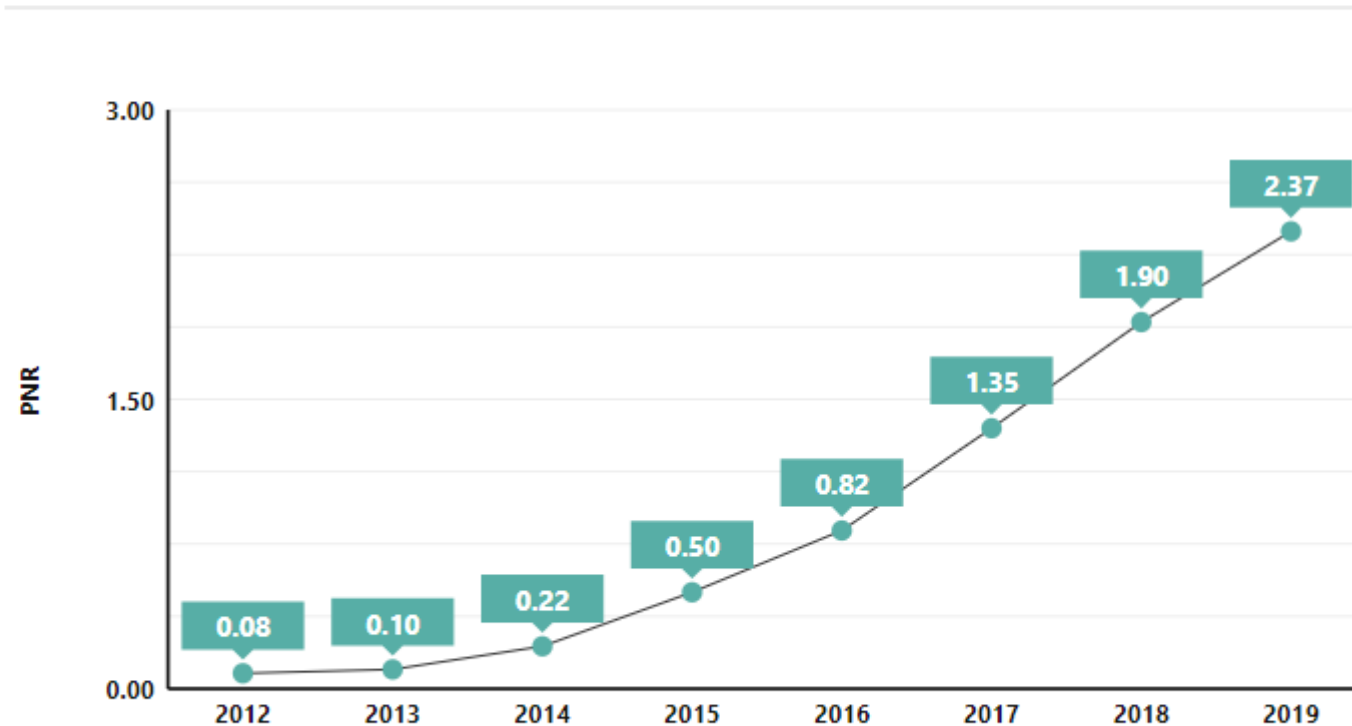
Aged 25-34: 2.42

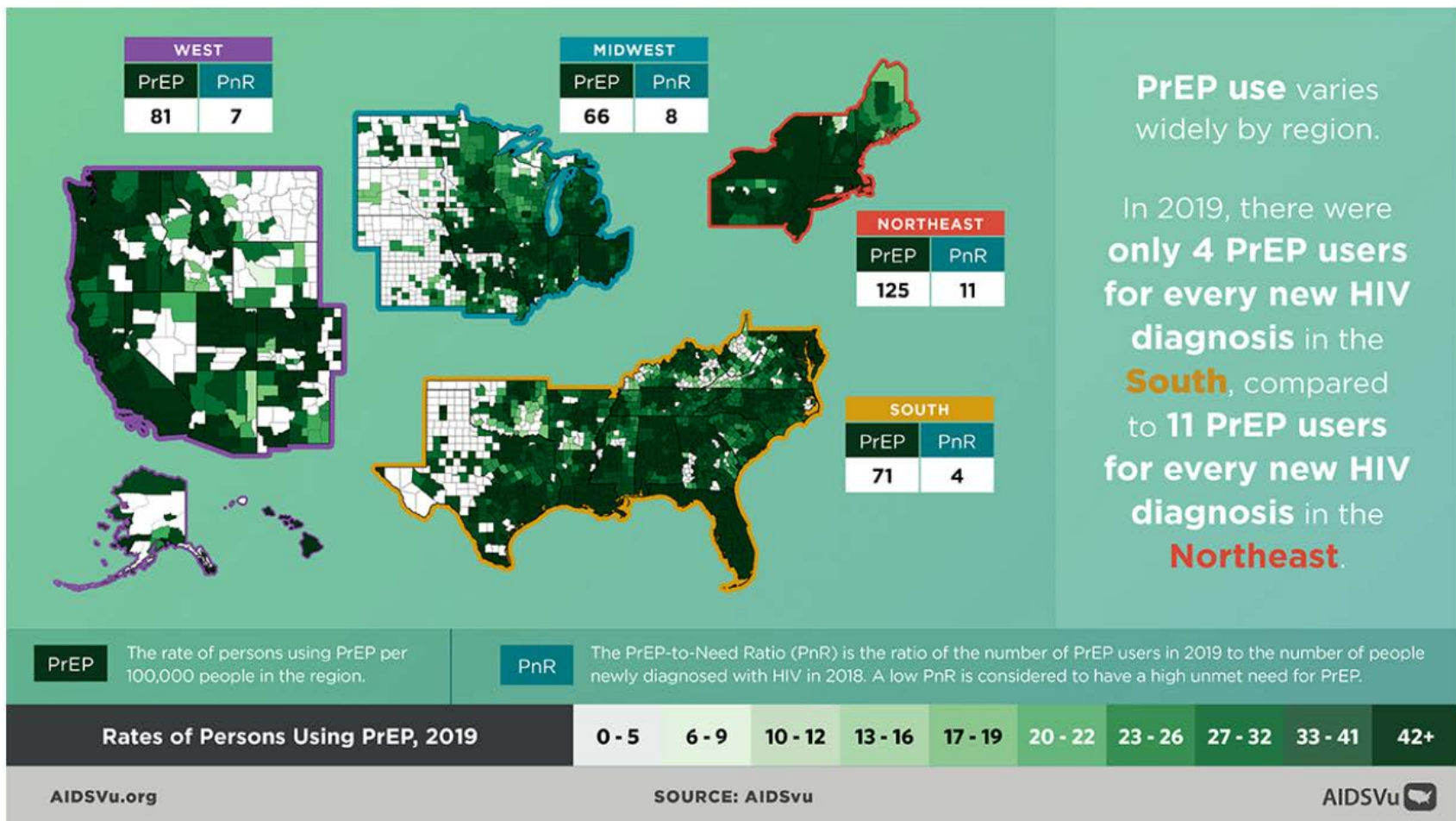
Aged 35-44: 3.05

Aged 45-54: 2.09

Aged 55+: 2.00

PNR, 2012-2019





- In 2019, the PnR for women (2.3) was a third of the PnR for men (6.9), indicating an inequity in PrEP use for women relative to their need

<https://aidsvu.org/resources/deeper-look-prep/>, accessed on 12/6/21

Providing PrEP

PrEP:
*HIV PREVENTION
WITH JUST
1 PILL A DAY*



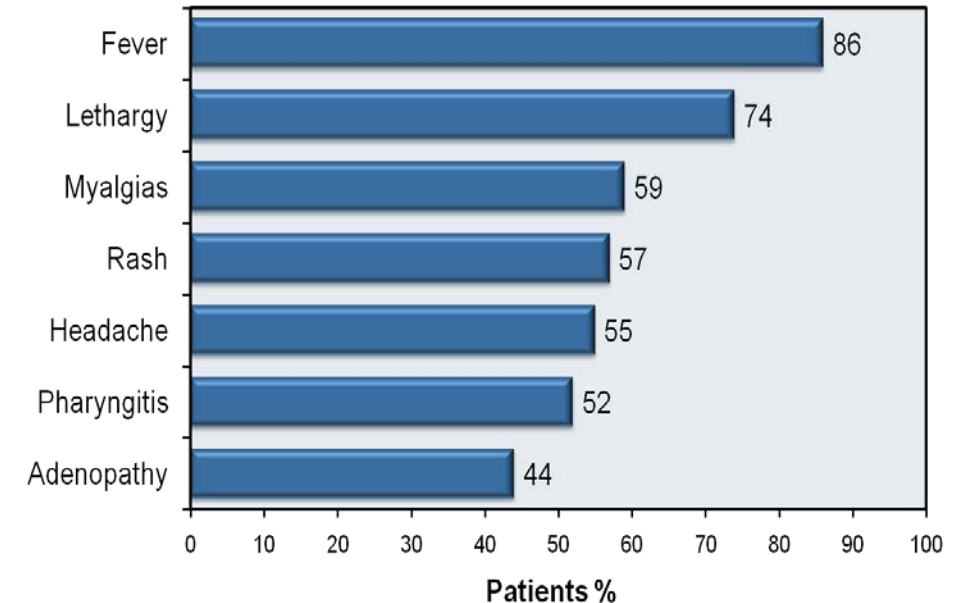
PrEP Checklist

- History
- Rule out HIV infection
- Baseline labs
- Patient counseling/education
- Rx

PrEP Checklist

☐ History

- PrEP indication(s)
- Consider PEP eligibility
- Current medications
- Hepatitis B
- Kidney disease
- Symptoms of acute HIV in the last 4-6 weeks



Vanhems P, et al. AIDS. 2000; 14: 375-81.

Who should be offered PrEP

CDC 2017 Guidelines

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Detecting substantial risk of acquiring HIV infection	<ul style="list-style-type: none"> HIV-positive sexual partner Recent bacterial STI[‡] High number of sex partners History of inconsistent or no condom use Commercial sex work 	<ul style="list-style-type: none"> HIV-positive sexual partner Recent bacterial STI[‡] High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network 	<ul style="list-style-type: none"> HIV-positive injecting partner Sharing injection equipment

Drafted CDC 2021 Guidelines *unpublished*

	Sexually-Active Adults and Adolescents ¹	Persons Who Inject Drugs
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: <ul style="list-style-type: none"> • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months² • History of inconsistent or no condom use with sexual partner(s) 	<ul style="list-style-type: none"> HIV-positive injecting partner OR Sharing injection equipment

² Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs

Candidates who should be offered PrEP include individuals who:

- Engage in condomless sex with partners whose HIV status is unknown, or who have untreated HIV, or who have unsuppressed virus while on treatment for HIV. [Smith, et al. 2012; Grov, et al. 2013].
- Are attempting to conceive with a partner who has HIV.
- Are at ongoing risk of HIV acquisition during pregnancy through inconsistent condom use with sex partners who have unsuppressed virus [Heffron, et al. 2016].
- Have, or are involved with partners who may have, multiple or anonymous sex partners.
- Engage in sexual activity at parties and other high-risk venues, or have sex partners who do so.
- Are involved, or have partners who may be involved, in transactional sex (i.e., sex for money, drugs, food, or housing), including commercial sex workers and their clients.
- Have been diagnosed with at least 1 bacterial sexually transmitted infection (STI) in the previous 12 months [Zetola, et al. 2009; LaLota, et al. 2011].
- Report recreational use of mood-altering substances during sex, including but not limited to alcohol, methamphetamine [Buchacz, et al. 2005; Zule, et al. 2007; Koblin, et al. 2011; Smith, et al. 2012; Grov, et al. 2013], cocaine, ecstasy, and gamma hydroxybutyrate.
- Report injecting substances or having sex partners who inject substances, including illicit drugs, hormones, or silicone.
- Are receiving non-occupational post-exposure prophylaxis (nPEP) and anticipate ongoing risk or have used multiple courses of nPEP [Heuker, et al. 2012].
- Request the protection of PrEP even if their sex partners have an undetectable HIV viral load (see the discussion of U=U, below).
- Self-identify as being at risk without disclosing specific risk behaviors.
- Acknowledge the possibility of or anticipate engaging in risk behaviors in the near future.

Do not withhold PrEP from candidates who:

- Are pregnant or planning a pregnancy.
- Use other risk-reduction practices inconsistently, including condoms.
- Report substance use.
- Have mental health disorders, including those with serious persistent mental illness.
- Report intimate partner violence.
- Have unstable housing or limited social support.
- Report a recent STI.
- Request PrEP even in they have a partner living with HIV with an undetectable viral load.

PrEP Checklist

History

- Rule out HIV infection
- Baseline labs
- Patient counseling/education
- Rx

PrEP Checklist

Rule out HIV infection

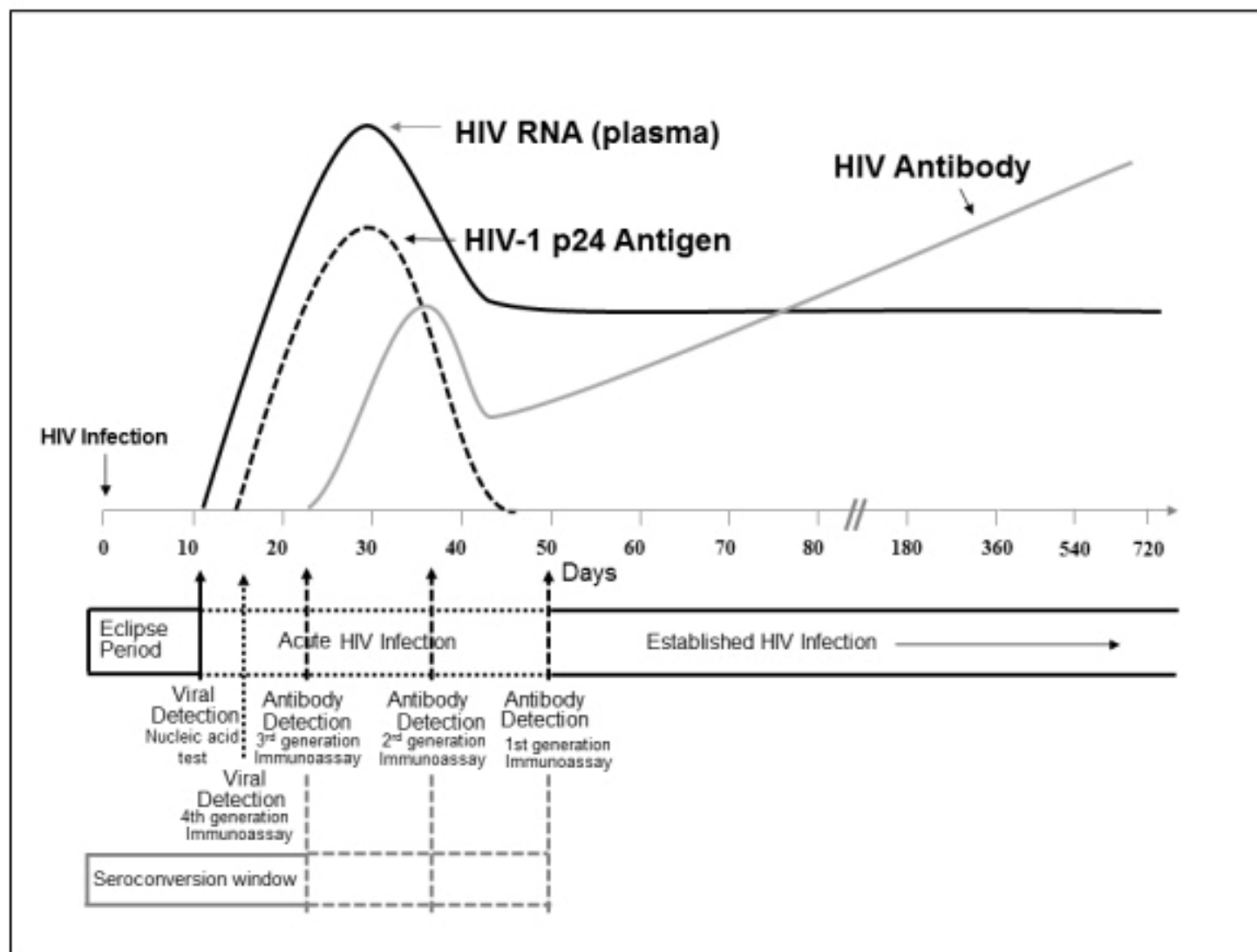
- Order a lab-based HIV 4th generation test even if a rapid POC result is negative
- In addition, order an HIV RNA if recent (within the last 4 weeks) high-risk exposure, or s/s of acute HIV infection “flu-like symptoms”
 - Fever
 - Lethargy
 - Myalgias
 - Rash
 - Headache
 - Pharyngitis
 - Lymphadenopathy

Types of HIV tests

- **Antibody-only**
 - ELISA, Western Blot
 - Multiple point-of-care (POC) options available
 - 3-12 weeks post-infection
 - IgM response begins around day 20, IgG day 30
 - 2 IgG/IgM sensitive POC tests available
- **Antigen/antibody (4th generation)**
 - p24 antigen/antibody combined immunoassay
 - **Recommended 1st step for HIV screening**
 - 2-6 weeks post-infection
 - P24 antigen is detectable in plasma by day 15, rises through day 30. Often cleared by day 50
 - First and only POC Ag/Ab test was approved in 2013, at least 4 lab-based Ag/Ab tests available
- **HIV-1 RNA (NAT)**
 - “Viral load”, qualitative or quantitative
 - 1-4 weeks post-infection
 - 50% have detectable plasma RNA within 12 days of infection, levels peak between 20-30 days



Figure 1. Sequence of appearance of laboratory markers for HIV-1 infection



Note. Units for vertical axis are not noted because their magnitude differs for RNA, p24 antigen, and antibody. Modified from MP Busch, GA Satten (1997)⁵⁰ with updated data from Fiebig (2003),⁴⁸ Owen (2008),⁴⁹ and Masciotra (2011, 2013).^{46,66}

Recommended HIV testing algorithm

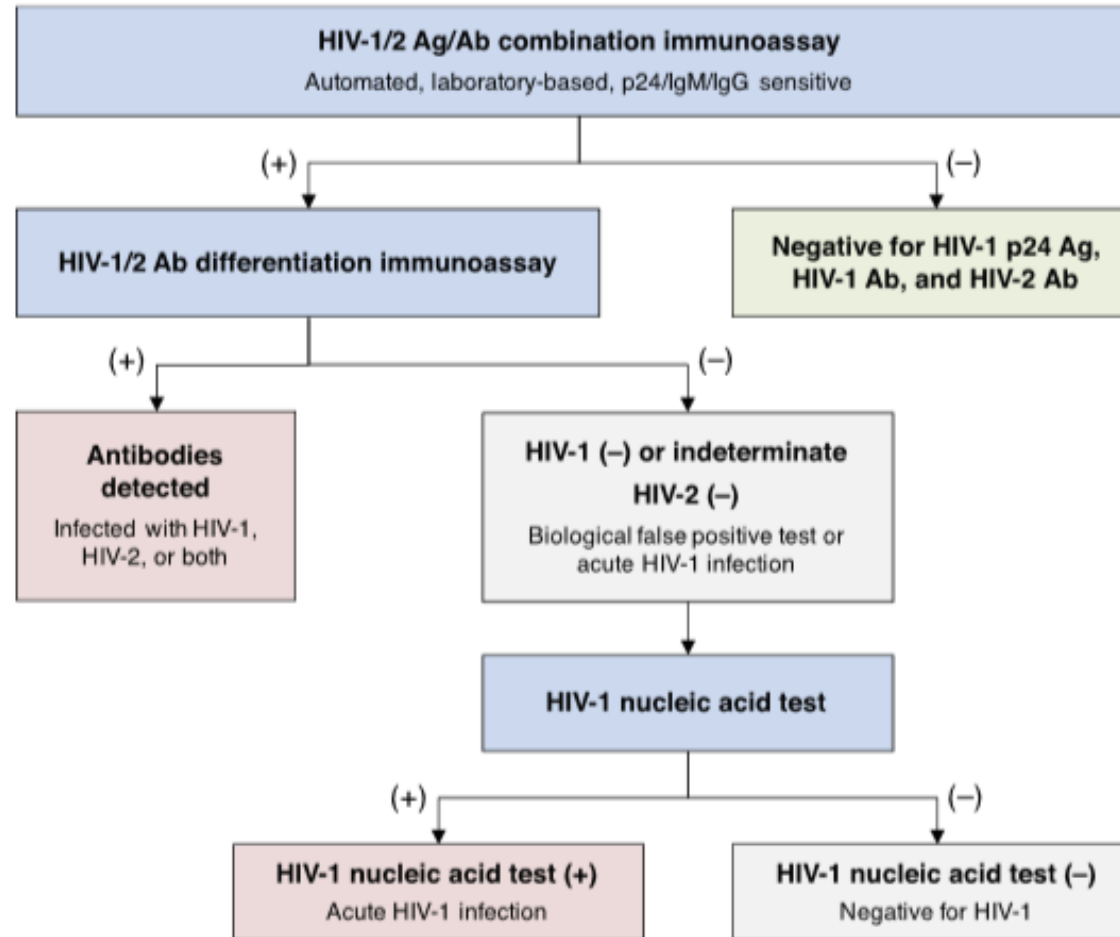


Figure 4. Recommended laboratory HIV testing algorithm. Any assay capable of reliably detecting p24 antigen (Ag) and both IgM and IgG antibodies (Ab) is the recommended starting point for HIV screening in the CDC algorithm, updated in 2014. Reactive specimens from the initial test are subjected to an IgG-sensitive supplemental immunoassay capable of differentiating HIV-1 from HIV-2; this step replaces the HIV-1 Western blot. Indeterminate or negative results from the differentiation test indicate either acute HIV infection (positive for p24 antigen or IgM antibody) or a biological false-positive test; the presence of detectable HIV RNA on a subsequent NAT is the arbitrator. Adapted from CDC.⁸

PrEP Checklist

- History
- Rule out HIV infection
- Baseline labs
- Patient counseling/education
- Rx

PrEP Checklist

Baseline labs

- HIV Ag/Ab (RNA prn)
- Metabolic panel (SCr) to calculate creatinine clearance
 - TDF/FTC should not be used if CrCl is $<60\text{mL/min}$
 - TAF/FTC should not be used if CrCl is $<30\text{mL/min}$
- HBsAg, anti-HBs, anti-HBc
- STI testing (GC/CT, Syphilis serology)
- Pregnancy test prn
- Take the opportunity to screen for HepC

PrEP Checklist

- History
- Rule out HIV infection
- Baseline labs
- Patient counseling/education
- Rx

PrEP Checklist

Patient counseling/education

- PrEP efficacy is highly dependent on adherence
- Time to protection:
 - Up to 1 week for receptive rectal exposure
 - Up to 3 weeks for all other exposure
- PrEP does not protect against other STIs. Encourage additional risk reduction
- Side effects are uncommon and usually resolve in the first month: headache and nausea can be managed by OTCs prn
- Discuss U=U for those in a discordant relationship
- Importance of routine follow up with HIV testing every 3 months
- Review how to navigate pharmacy refills and pay for PrEP

PrEP Checklist

- History
- Rule out HIV infection
- Baseline labs
- Patient counseling/education
- Rx

HIV Lifecycle & major classes of HIV medications

NRTI

Nucleoside reverse transcriptase inhibitor

NNRTI

Non-nucleoside reverse transcriptase inhibitor

PI

Protease inhibitor

INSTI

Integrase inhibitor

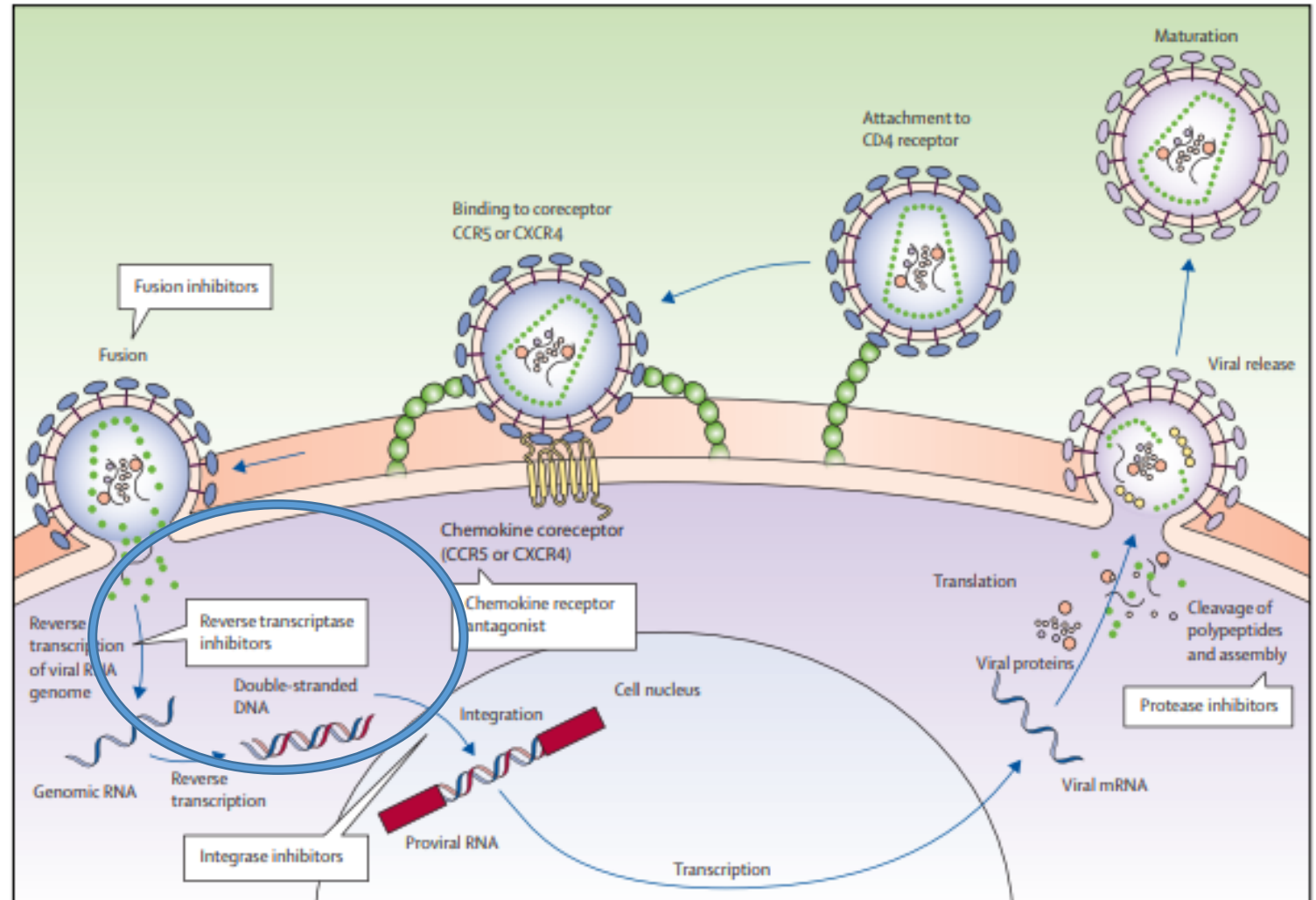


Figure 2: HIV life cycle showing the sites of action of different classes of antiretroviral drugs
Adapted from Walker and colleagues,³⁶ by permission of Elsevier.

Medications currently used for PrEP

Drug name	Abbreviation	Combination (Brand) tablets
tenofovir alafenamide	TAF	TAF/FTC (Descovy) TDF/FTC (Truvada)
tenofovir disoproxil fumarate	TDF	
emtricitabine	FTC	



TDF vs. TAF

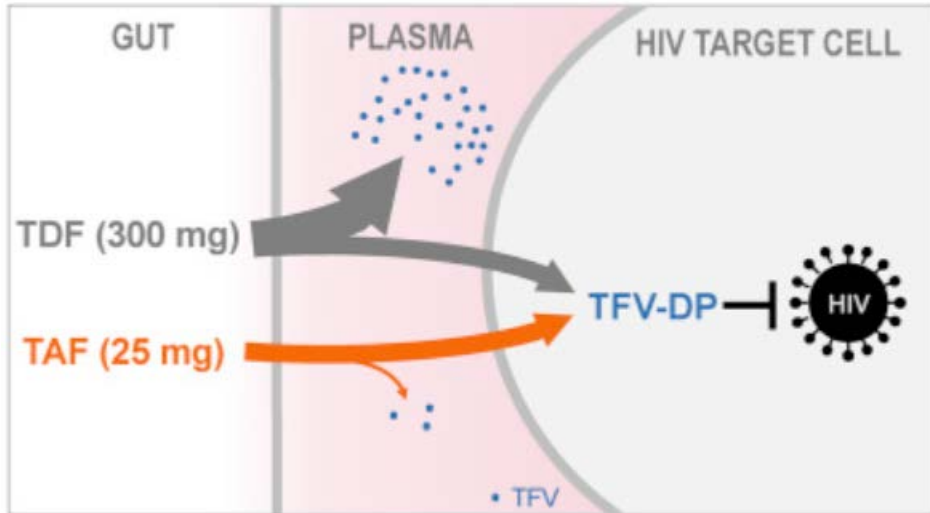


Fig. 3. Comparison of the efficiency of HIV-target cell delivery following oral administration of tenofovir prodrugs. Oral administration of TAF at 25 mg, 1/10th the molar equivalents of TFV present in 300 mg TDF, results in 90% lower systemic levels of TFV while maintaining intracellular levels of the pharmacologically active metabolite TFV-DP in HIV-target cells.

- TDF has been administered extensively (>9 million patient years) as a preferred backbone of HIV therapy
- Tenofovir diphosphate is the active drug, once in cells
- Tenofovir alafenamide more efficiently deliver tenofovir to target cells resulting in 90% lower systemic exposure
- Renal and bone toxicity observed with TDF is associated with high circulating plasma levels of tenofovir

TAF/FTC for PrEP

- Studied only in HIV-negative MSM and transgender women who have sex with men at high risk for HIV (total n = 5,387) in one RCCT ¹
- Non-inferior to TDF-FTC
- Incremental improvements in renal and bone measures but clinical impact not demonstrated; no serious toxicities reported with TDF/FTC for PrEP
- FDA approved in 2019 for HIV prevention for sexual exposures EXCEPT vaginal receptive sex.
- Insufficient data for use among heterosexual cis-gender women, transgender men, people who inject drugs, people who use 2-1-1 (on-demand) PrEP






1. Mayer et al. 2020 Lancet 396(10246): 239-254

PrEP Checklist

Rx

- TDF/FTC (Truvada) 300/200mg 1 tablet by mouth once daily
- TAF/FTC (Descovy) 25/200mg 1 tablet by mouth once daily
- Take with or without food
- On demand dosing 2-1-1, not in CDC guidelines
 - 2 tablets of TDF/FTC 2-24 hours before sex, then 1 tab 24 hours later, and another 1 tab 24 hours later
- No more than 90 days at a time
 - For example: #30, 2 refills

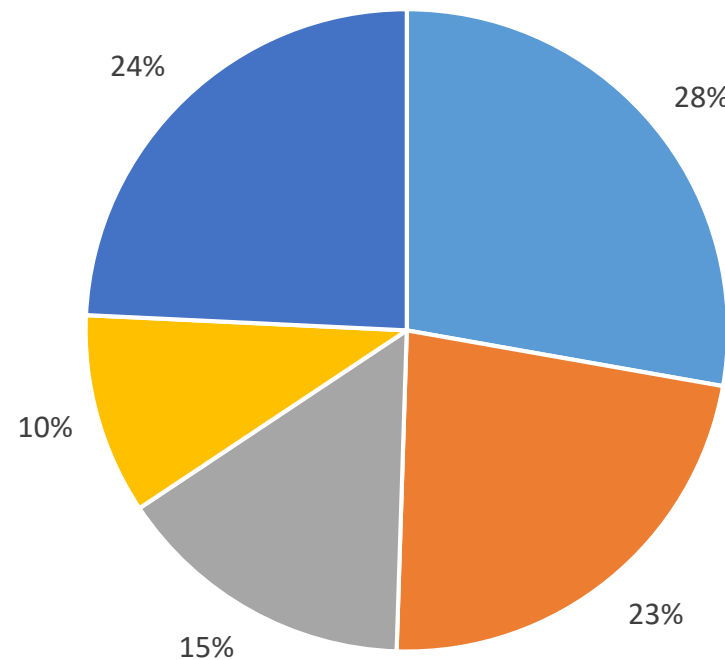
PrEP Checklist

-  History
-  Rule out HIV infection
-  Baseline labs
-  Patient counseling/education
-  Rx

BCHD Patient survey: Difficulty starting PrEP

57% reported some difficulty related to filling the first prescription

N=40



■ I didn't have insurance coverage

■ I had problems getting my Rx filled

■ The clinic visit took too long

■ The Rx copay was too high

■ No difficulty

Paying for PrEP

Gilead Advancing Access

<https://www.gileadadvancingaccess.com/>

- Co-pay Coupon Program
 - For those with copays through private insurance
 - up to \$7,200/yr
 - Enroll online or over the phone, immediate co-pay card to print or save, then show to the pharmacy
- Medical Assistance Program
 - For uninsured individuals, regardless of immigration status
 - Income limit 500% FPL, need to submit proof of income

ADVANCING
ACCESS®

AFFORDING
YOUR MEDICINE

UNDERSTANDING YOUR
COVERAGE

UNINSURED 24/7 SUPPORT

Gilead's Advancing Access® Program Is Here to Help You

Gilead's Advancing Access program is committed to helping you afford your medication no matter your situation. Whether you have insurance or not, we can explore potential coverage options that might be right for you.

Our dedicated program specialists are here to help you. Talk to someone right away by calling **1-800-226-2056**. Advancing Access phone lines are open M - F 9am - 8pm ET. If you reach us after hours, leave a message, and we will call you back during the next business day.

The Advancing Access CO-PAY COUPON PROGRAM



The Advancing Access PATIENT SUPPORT PROGRAM



<https://www.gileadadvancingaccess.com/>

Rapid/Same-day/Immediate PrEP

- Start PrEP while awaiting test results
 - IF:
 - Point-of-care HIV test is negative
 - No symptoms of acute HIV in the last 6 weeks
 - No hx of renal disease or HepB
 - No exposures in the last 72 hours warranting PEP
- Engage patients more fully in care and reduce exposures to HIV while awaiting test results
- Some risk for starting a non-suppressive ART regimen on someone with HIV
- Consider strategies to ensure you will be able to stop PrEP if there are medical contraindications based on initial lab results

Rapid PrEP cont'd

Denver STD clinic

- 100 individuals \geq 18 y/o (98% were cis-male MSM)
- Received 30-day starter pack, linked to ongoing PrEP care
 - POC HIV Ag/Ab, and urine HCG prn
 - Labs: SCr, HepB, HIV RNA prn
 - Contact with abnormal results in 2 days
- Results:
 - 78% attended at least one follow-up visit
 - 57% attended at least 2 f/u visits
- **Conclusion**
 - **Same-day PrEP is acceptable, feasible and safe**

Kamis KF, et al. Open Forum Infectious Diseases. June 2019

NYC STD Clinics, Jan 2017-June 2018

- Cis-gender men and women >18
- 30-day supply given, linked to outside PrEP provider
- 1387 qualified for immediate PrEP (96.5%)
 - 4 had an absolute contraindication and discontinued within 10 days (0.2%)
 - of those with no contraindications but who delayed PrEP initiation, only 35% actually initiated within 60 days
- **Conclusions:**
 - Very few rapid PrEP patients needed to discontinue due to medical contraindications
 - **Delaying PrEP initiation resulted in substantial loss to follow up**

Mikati T, Jamison K, Daskalakis DC. CROI abstract, March 2019

PrEP during pregnancy

- HIV acquisition is higher during pregnancy
- Risk of perinatal transmission is significantly higher during acute seroconversion when a patient is pregnant or breastfeeding
- PrEP is indicated for those at ongoing risk of HIV acquisition during pregnancy through inconsistent condom use with sex partners who have unsuppressed virus
- Do not withhold PrEP from those who are pregnant or planning a pregnancy
- Tenofovir disoproxil fumarate (TDF) in combination with emtricitabine (FTC) is a preferred NRTI combination for use in treatment naïve pregnant women with HIV
(<https://clinicalinfo.hiv.gov/en/guidelines/perinatal/overview-2>)
- TAF/FTC is not approved for use as PrEP during pregnancy

Future of PrEP delivery

- Injectable cabotegravir q8 weeks
 - HPTN 084 RTC comparing CAB LA to TDF/FTC in sexually active women at risk for HIV. Estimated study completion date May 2022
- Pharmacist-delivered PrEP
 - State-dependent
- Nurse-led PrEP models
- Telehealth options

<https://clinicaltrials.gov/ct2/show/results/NCT03164564>, accessed 12/7/21

Guidelines

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2017 UPDATE

A CLINICAL PRACTICE GUIDELINE

Updated federal guidelines coming soon

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE



**CLINICAL
GUIDELINES
PROGRAM**

<https://www.hivguidelines.org/>

Resources

Current PrEP guidelines (stay tuned for the 2021 update)

<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

Current nPEP guidelines

<https://stacks.cdc.gov/view/cdc/38856>

New York State clinical guidelines, includes HIV, PEP and PrEP

<https://www.hivguidelines.org/>

Paying for PrEP

<https://www.nastad.org/prep-access/prep-assistance-programs>

I like this resource for webinars, one-day in person conferences, and guidelines.

<https://www.iasusa.org/>

My favorite ID blog, especially his "really rapid review" after big HIV/ID conferences

<https://blogs.jwatch.org/hiv-id-observations/>

Warm line consultation from UCSF, also great resources

<https://nccc.ucsf.edu/>

My contact info

Sarah Rives

sarah.rives@baltimorecity.gov

443-826-8219