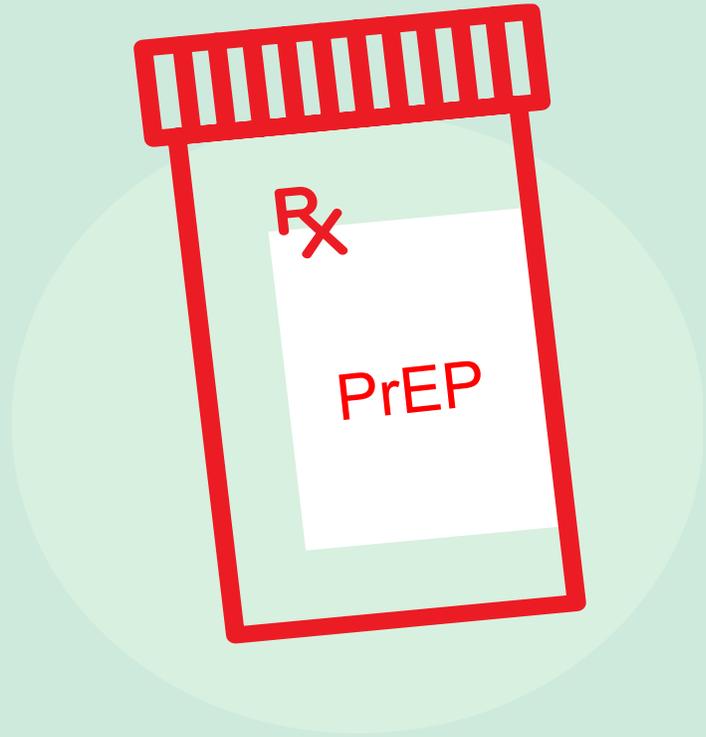


# What you need to know about PrEP



# | Collaborators



Milken Institute School  
of Public Health

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THE GEORGE WASHINGTON UNIVERSITY

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*GEORGETOWN UNIVERSITY*



More resources available at the DC Center for Rational Prescribing

[doh.dc.gov/dcrx](https://doh.dc.gov/dcrx)

# | Presenters



- Sarah Calabrese, PhD
- Adriane Fugh-Berman, MD
- Travis Gayles, MD, PhD
- Shawnika Hull, PhD
- Susan Wood, PhD

# Course Faculty



- Paul Bellman, MD
- Sarah Calabrese, PhD
- Adriane Fugh-Berman, MD
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- Kofi Onumah, PharmD, RPh
- Tayiana Roussell-Reed, PharmD, MS, AAHIVP, RPh
- Susan Wood, PhD

# Important Information

-  The video will progress at its own pace.
-  Do not attempt to speed up the video.
-  The post-test will only unlock after viewing the entire video.
-  The video can be paused and resumed later.

# Course Objectives



1. List various prevention methods of HIV.
2. Determine which patients benefit most from PrEP therapy.
3. List common and serious adverse effects of PrEP.
4. Describe the recommended labs and follow-up appointment schedule for patients using PrEP.

# HIV Prevention Strategies



# HIV prevention strategies

1

## REDUCE INFECTIOUSNESS OF THOSE WITH HIV

- Lower viral load = Lower risk of transmission

2

## REDUCE EXCHANGE OF BODILY FLUIDS

- Physical barriers to reduce contact with the virus

3

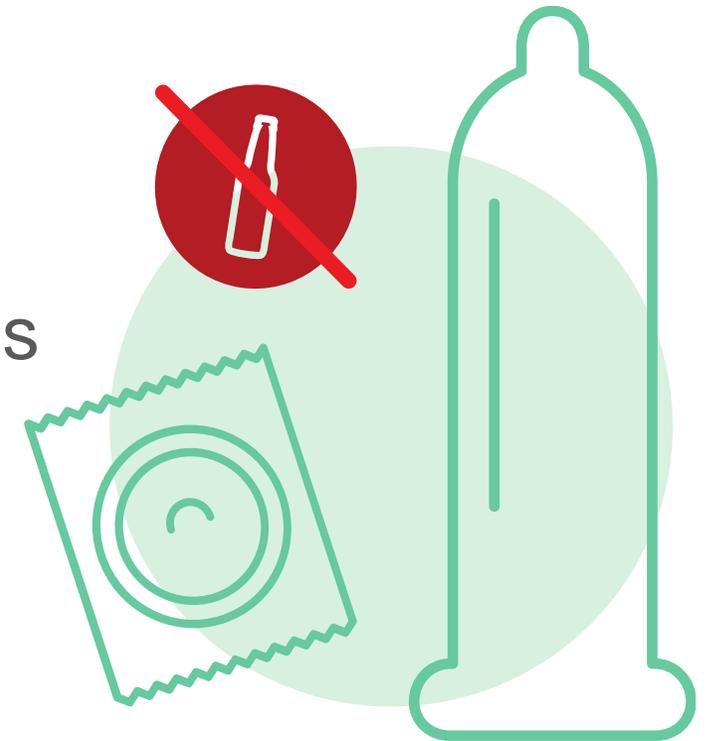
## REDUCE SUSCEPTIBILITY TO HIV INFECTION

- Biological mechanisms of prevention



# HIV prevention tools

- Male and female condoms
- Clean works for IV drug use (needles, syringes, spoons, etc.)
- HIV treatment for HIV positive individuals
- Abstinence
- Sober sex
- Mental health treatment
- Regular HIV testing
- Wraparound services (food, housing, healthcare)



# Treatment as prevention

- Treatment is a highly effective form of prevention
- Viral suppression in HIV positive patients can prevent transmission

**93%** reduction in transmission in HIV Prevention Trial Network 052



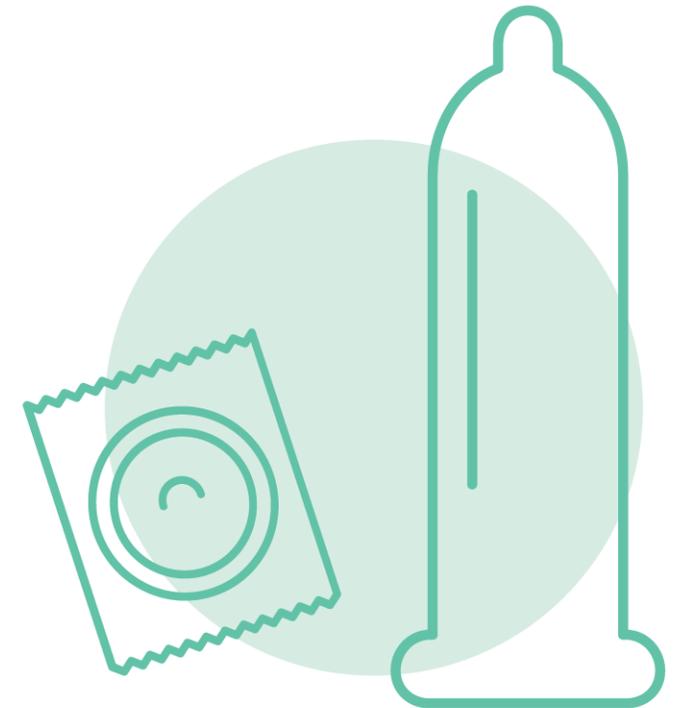
The NEW ENGLAND  
JOURNAL of MEDICINE

## Antiretroviral Therapy for the Prevention of HIV-1 Transmission

M.S. Cohen, Y.Q. Chen, M. McCauley, T. Gamble, M.C. Hosseinipour, N. Kumarasamy, J.G. Hakim, J. Kumwenda, B. Grinsztejn, J.H.S. Pilotto, S.V. Godbole, S. Chariyalertsak, B.R. Santos, K.H. Mayer, I.F. Hoffman, S.H. Eshleman, E. Piwowar-Manning, L. Cottle, X.C. Zhang, J. Makhema, L.A. Mills, R. Panchia, S. Faesen, J. Eron, J. Gallant, D. Havlir, S. Swindells, V. Elharrar, D. Burns, T.E. Taha, K. Nielsen-Saines, D.D. Celentano, M. Essex, S.E. Hudelson, A.D. Redd, and T.R. Fleming, for the HPTN 052 Study Team\*

# Condoms

- Consistent use of condoms for all acts of penetrative vaginal intercourse reduced HIV incidence by 80% in heterosexual serodiscordant couples. (Weller 2012)
- For men who reported having anal sex with an HIV-positive male partner, “always” using condoms was 70% effective. (Smith 2015)
  - There was no significant protection with “sometimes” condom use.



# HIV Transmission Varies by Type of Sex

PrEP reduce the risk for all kinds of sexual contact.

Anal  
sex

Vaginal  
sex

Oral sex

- With men
- With women

# What is PrEP?



# PrEP=Pre-Exposure Prophylaxis

- Antiretroviral medication taken daily to prevent HIV
- Truvada, a combination of tenofovir (TDF) and emtracitibine (FTC), was approved as PrEP by the FDA in 2012



# PrEP vs. PEP



PrEP = PRE-EXPOSURE  
PROPHYLAXIS

- Initiated before exposure to risk
- Taken daily for as long as a patient is at risk for HIV to provide ongoing protection

VS

PEP = POST-EXPOSURE  
PROPHYLAXIS

- Taken within 72 hours after exposure or suspected exposure and daily for 28 days



# TDF Alone is Effective



- TDF was just as effective as TDF/FTC in a randomized placebo-controlled trial of TDF and TDF/FTC of 4,410 serodiscordant heterosexual couples in Kenyan and Uganda. (Baeten 2014)

# Generic Options for PrEP



- When generic TDF becomes available (expected in 2017), it can be combined with branded FTC. This would save money.
- The DHHS Guidelines panel considers 3TC (currently available as a generic) interchangeable with FTC.

# Tenofovir Alafenamide (TAF)



- A multi-drug formulation containing TAF caused smaller creatinine increases and less loss of bone mineral density (spine and hip) than a multi-drug formulation containing TDF. (Sax 2015)
- TAF is not yet approved for PrEP.
  - TAF/FTC became available in 2016 for HIV treatment.
  - An RCT for TAF/FTC for PrEP began in 2016.
  - TAF may result in lower levels of tenofovir in muscoa and genital fluids. (Garrett 2016)

# Men who have sex with men (MSM)— placebo-controlled trials of PrEP



Study	Treatment	Efficacy estimate	Efficacy in Adherent Participants	Quality of Evidence
iPrEx Trial (2010)	TDF/FTC (n=2499)	44%	92% (40-99%)	High

Adapted from CDC 2014 Guidelines on PrEP

# PROUD study



- In an open-label randomized trial of 544 HIV-negative men who had unprotected anal intercourse, patients received PrEP immediately or after 1 year.
- HIV incidence was significantly lower in the immediate group (1.2 cases per 100 person years) compared to the delayed group (9.0 per 100 person years).
  - The proportional reduction in risk was 86%.

(McCormack 2016)

# | On-Demand Dosing



- Using PrEP sporadically is ineffective.
- However, on-demand (intermittent) use can be very effective if a specific regimen is followed.

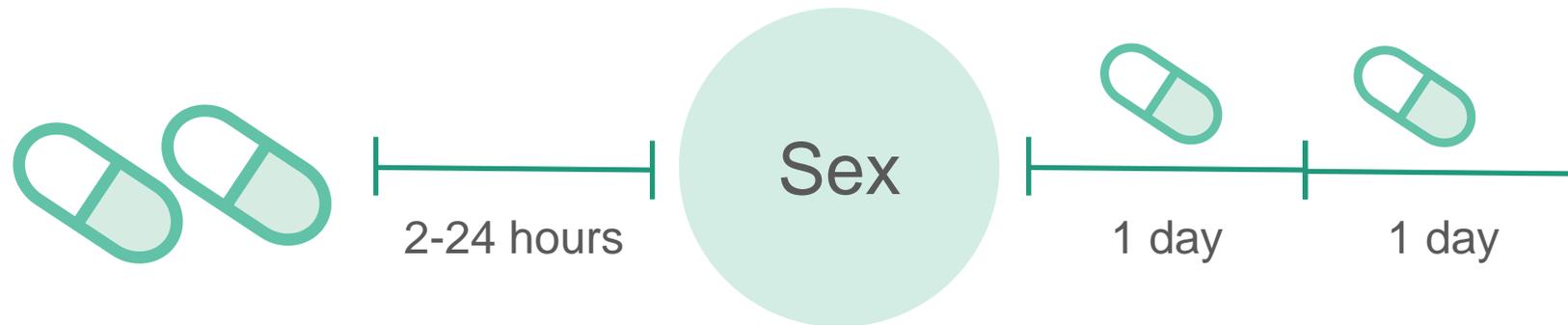
# On-Demand PrEP in Men who have sex with men (MSM)



- Intermittent (“on-demand”) TDF/FTC was tested in 400 MSM men who had unprotected anal sex with at least two partners in the previous 6 months.
- Patients were instructed to take two pills 2-24 hours before sex, then one pill daily until two days following the last act.
- The relative reduction of HIV transmission was 86%. (Molina 2015)

# On-Demand PrEP in Men who have sex with men (MSM)

- Intermittent (“on-demand”) TDF/FTC reduced HIV transmission by 86% in men who have unprotected anal sex. (Molina 2015)



Two pills 2-24 hours before sex, then one pill daily until two days after the last sex act.

# Heterosexual men and women— placebo-controlled trials

Study	Treatment	Efficacy estimate		Efficacy in Adherent Participants	Quality of Evidence
		TDF	TDF/FTC		
Partners PrEP (2012)	TDF, TDF/FTC (n=4,758) 36 months	All: 67% Women: 71% Men: 63%	All: 75% Women: 66% Men: 84%	TDF: 86% (67%-94%) TDF/FTC: 90% (58-98%)	High
TDF2 (2012)	TDF/FTC (n=1,219) 1.1 years	All: 63% Women: 49% (NS) Men: 80%		Women: 75% Men: 82%	Moderate

NS=not statistically significant

Adapted from CDC 2014 Guidelines on PrEP

# Heterosexual Women— placebo-controlled trials

Study	Treatment	Efficacy estimate		Quality of Evidence
FEM-PrEP (2012)	TDF/FTC (n=2,120)	6% (NS)		Low
West African Trial (2007)	TDF (n=936)	65% (NS)		Low
VOICE (2015)	TDF, TDF/FTC (n=3,019)	TDF -50% (NS)	TDF/FTC -4% (NS)	Low

NS=not statistically significant

Adapted from CDC 2014 Guidelines on PrEP

# Transgender women

- A subgroup analysis of 339 transgender women in iPrEx found no difference between PrEP and placebo in the number of people who seroconverted.
  - [In patients on PrEP,] HIV incidence was zero if drug was detected, and 4.9 per 100 person-years if drug was not detected.

(Deutsch 2015)

# Intravenous Drug Users (IVDU)



Study	Treatment	Efficacy estimate	Efficacy in Adherent Participants	Quality of Evidence
BTS (2013)	TDF (n=2,411)	All: 49% Women: 78.6% Men: 37.6% (NS)	74% (17-94%)	High

NS=not statistically significant

Adapted from CDC 2014 Guidelines on PrEP

# Adverse Effects of PrEP



# Common adverse effects of PrEP (usually transient)



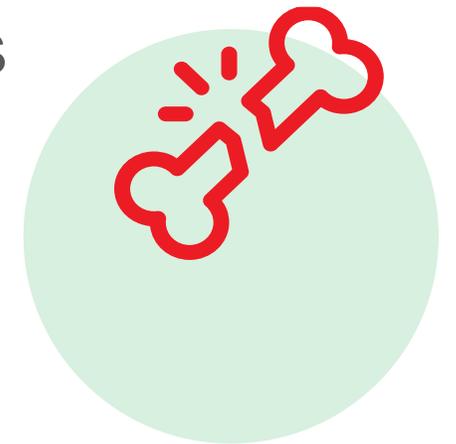
# Serious adverse effects of PrEP

- Loss of bone mass
- Renal impairment (New onset or worsening)
  - Acute kidney failure
  - Fanconi syndrome
- Lactic acidosis
- Liver function abnormalities, worsening of hepatitis
- Severe hepatomegaly with steatosis
- Acute exacerbation of Hepatitis B post-treatment
- Risk of drug resistance



# Bone Density

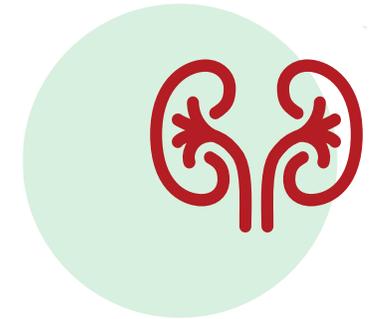
- In a study of 221 people, subjects treated with TDF/FTC for a median of 1.1 years experienced a significant decline in bone mineral density in the forearm, hip, and lumbar spine. (Thigpen 2012)
- The long-term effect of PrEP on younger patients who have not achieved their adult bone mineral density is unknown.
- Baseline and follow up bone densitometry may be prudent.



# Renal Function

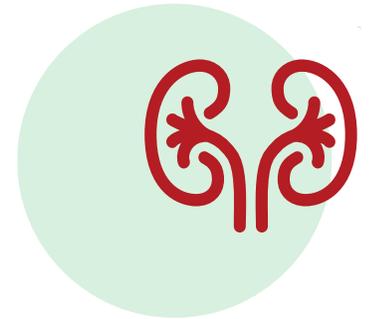
- An observational Veterans Administration study of 10,841 HIV-positive patients found that each year of exposure to tenofovir treatment was associated with:
  - 33% increased risk of chronic kidney disease
  - 11% increased risk of rapid decline in kidney function
  - 34% increased risk of time to first occurrence of proteinuria
  - Median follow up ranged from 3.9 years (proteinuria) to 5.5 years (chronic kidney disease).

(Scherzer 2012)



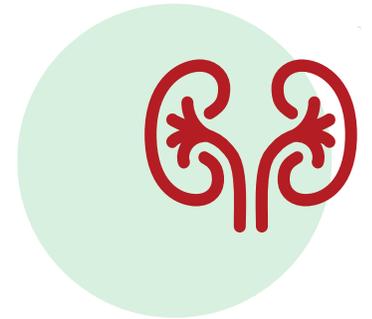
# Renal Function

- In 3,924 highly adherent individuals who took TDF-based PrEP for a median of 36 months, PrEP reduced mean estimated glomerular filtration rate (eGFR); the effect reversed weeks after discontinuation.
  - All subjects had creatinine clearance  $\geq 60$  mL/min at baseline
  - 98% started with eGFRs  $\geq 90$  mL/min
    - Creatinine-based eGFR estimates are less accurate in people with wasting or loss of muscle mass
  - Proteinuria was not assessed (Mugwanya 2016)
- Patients on TDF should be screened prior to treatment and followed every six months with serum phosphates and urine microalbumin.
  - Protein detected on routine urine dipstick is insufficient to pick up TDF-related nephrotoxicity.



# Renal Function

- The long term potential effects of tenofovir on the kidneys is not yet known and requires further research.
- Any rise in creatinine in a patient on PrEP is reason for concern.
  - Irreversible kidney damage may have occurred by the time serum creatinine levels rise.
- Nephrologists strongly advise monitoring serum phosphates and urine microalbumin.
- When creatinine clearance is less than 60 mL/min, TAF/FTC should be considered.



# Who is eligible for PrEP?



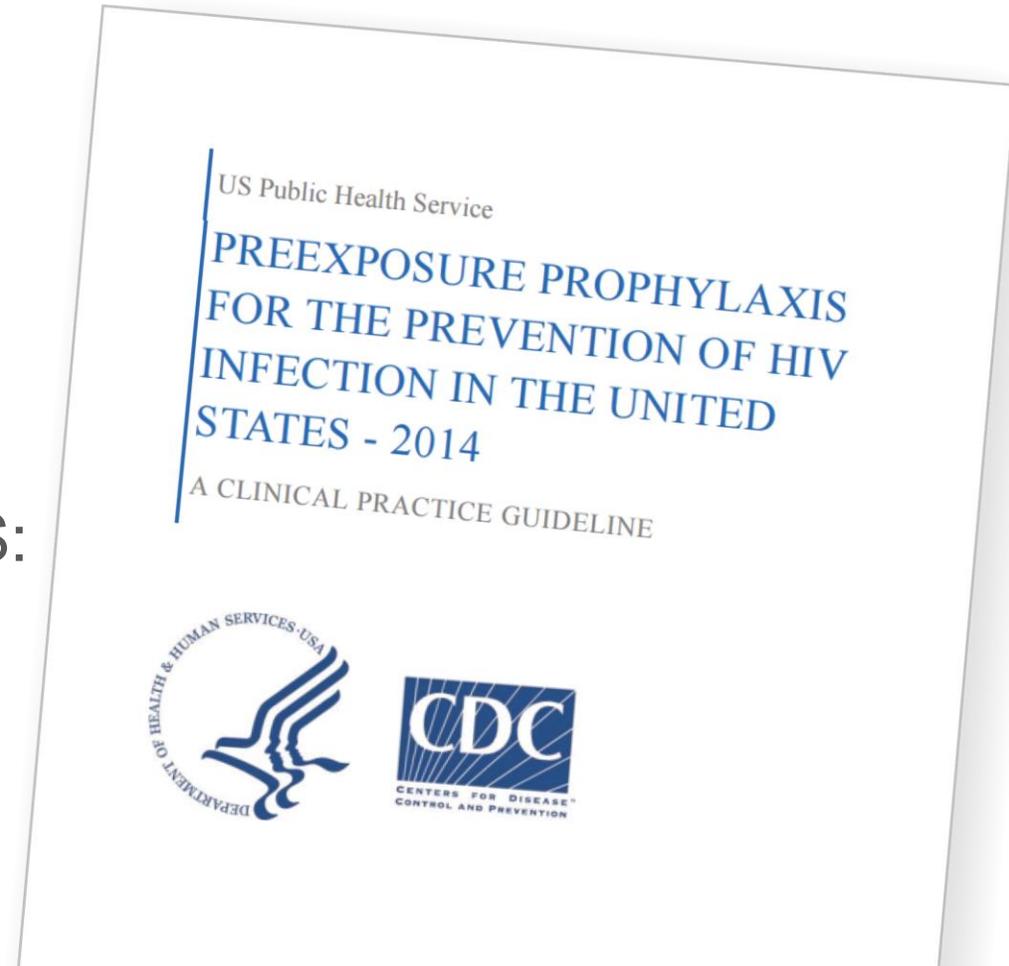
# CDC Guidelines

## SEX-RELATED CONSIDERATIONS:

- recent condom (non)use
- history of STI
- number of partners
- partner HIV status

## DRUG-RELATED CONSIDERATIONS:

- Injection/treatment history
- Equipment sharing
- Sexual risk



# Summary of guidance



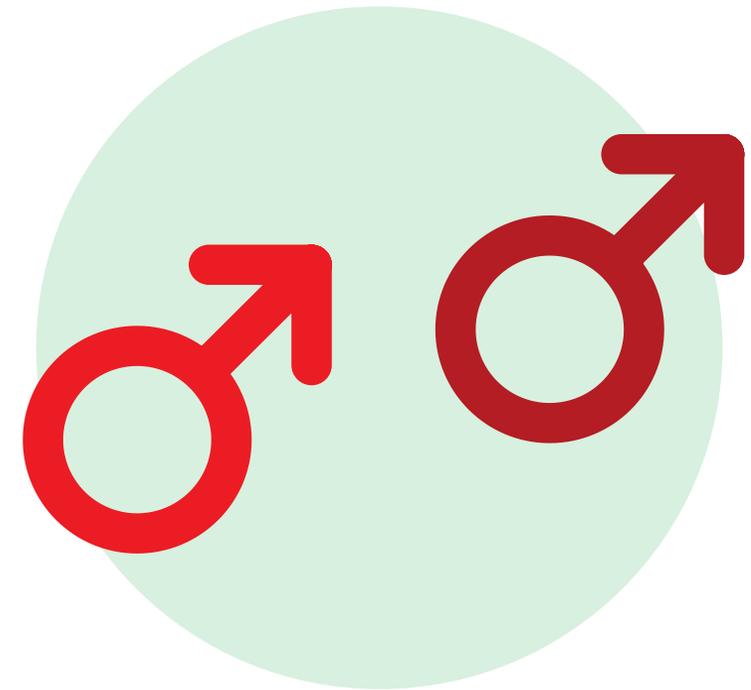
	Men who have sex with men	Heterosexual men and women	Injection drug users
Detecting substantial risk of acquiring HIV infection	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Recent bacterial STI</li> <li>• High number of sex partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>
Clinically eligible	<ul style="list-style-type: none"> <li>• Documented negative HIV test result before prescribing PrEP</li> <li>• No signs/symptoms of acute HIV infection</li> </ul>	<ul style="list-style-type: none"> <li>• Normal renal function; no contraindicated medications</li> <li>• Documented hepatitis B virus infection and vaccination status</li> </ul>	
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	<ul style="list-style-type: none"> <li>• Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment</li> <li>• At 3 months and every 6 months thereafter, assess renal function</li> <li>• Every 6 months, test for bacterial STIs</li> </ul>		
	<ul style="list-style-type: none"> <li>• Do oral/rectal STI testing</li> </ul>	<ul style="list-style-type: none"> <li>• Assess pregnancy intent</li> <li>• Pregnancy test every 3 months</li> </ul>	<ul style="list-style-type: none"> <li>• Access to clean needles/syringes and drug treatment services</li> </ul>

More information: <https://www.cdc.gov/hiv/risk/prep/>

# Men who have sex with men

## AT LEAST ONE OF THE FOLLOWING

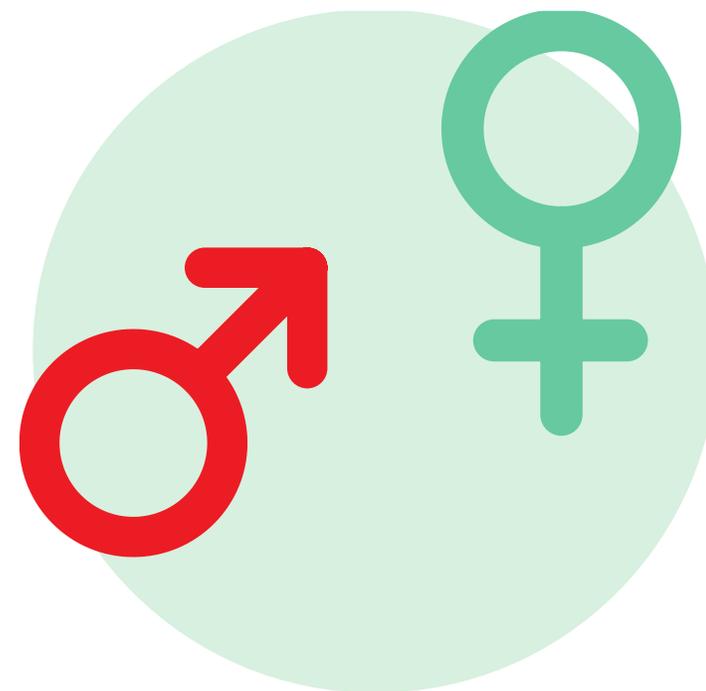
- Any anal sex without a condom in the past 6 months
- Any STI diagnosis in the past 6 months
- In a relationship with an HIV positive partner



# Men who have sex with women

## AT LEAST ONE OF THE FOLLOWING

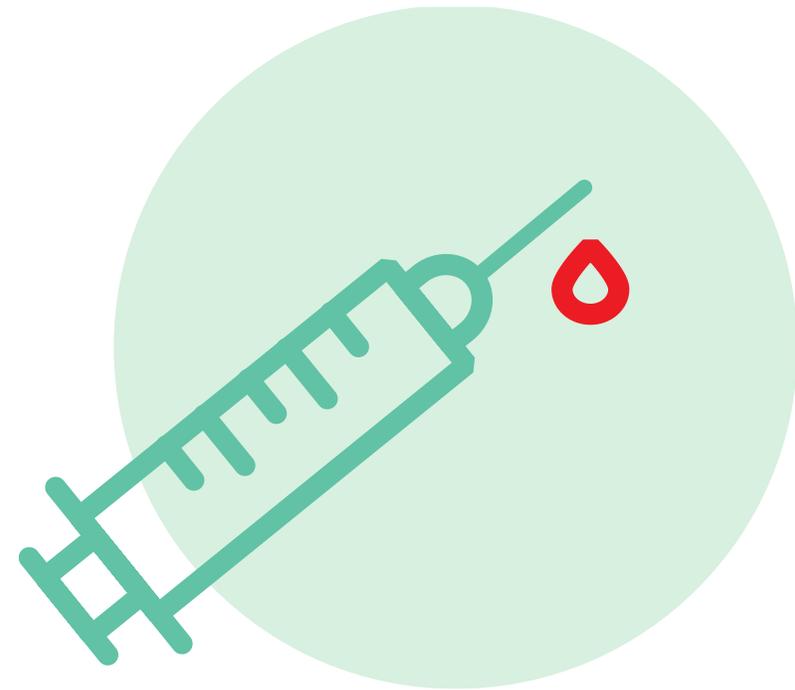
- Infrequent condom use with one or more partners of unknown HIV status who are known to be at substantial risk for HIV
- In a relationship with an HIV-positive partner
- A man who has sex with women and men



# Drug injection users

## AT LEAST ONE OF THE FOLLOWING

- Any sharing of injection or drug preparation equipment in past 6 months
- Participation in a methadone, buprenorphine, or suboxone treatment program in the past 6 months
- Risk of sexual acquisition



# Other considerations

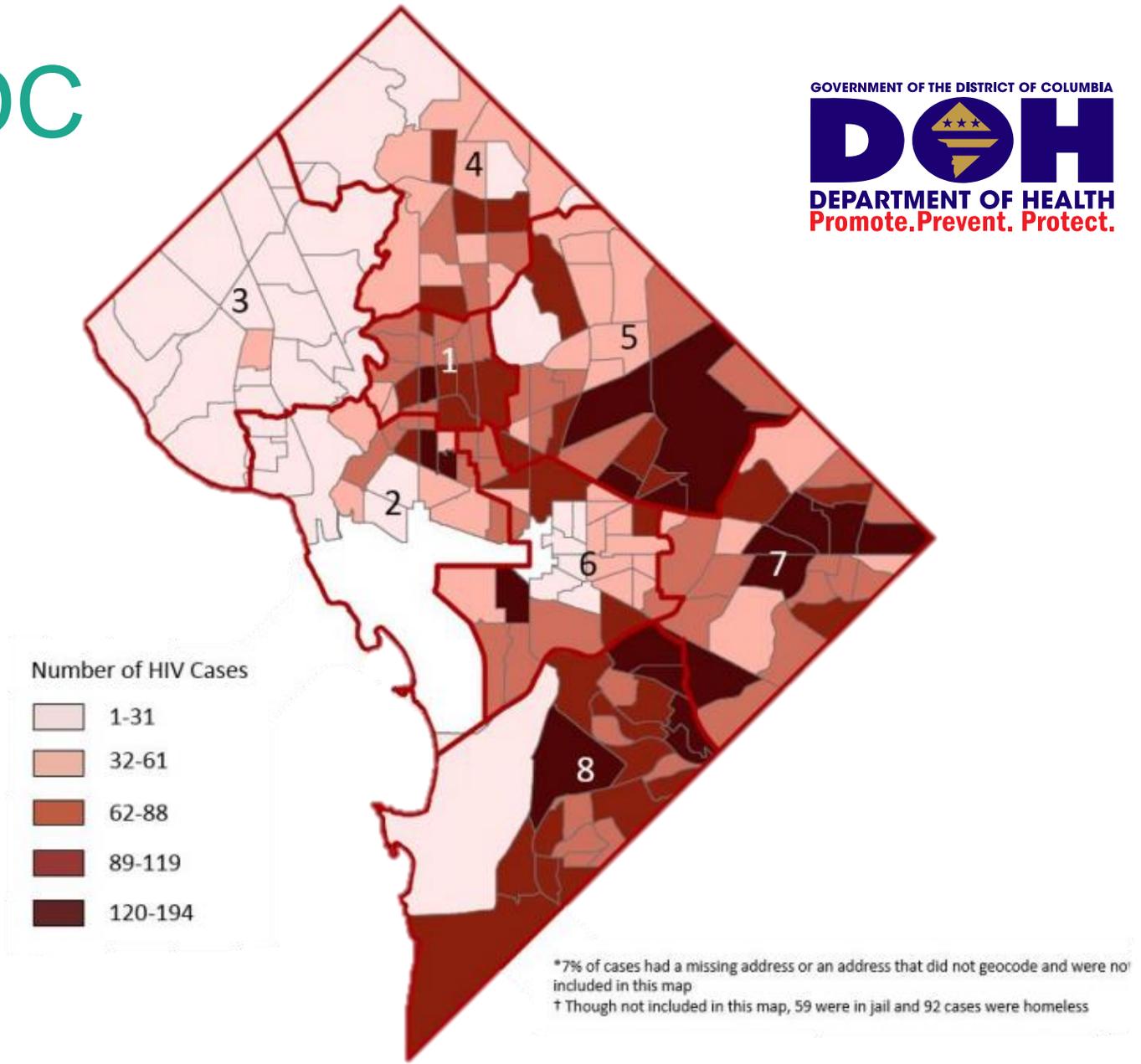


- Repeated PEP use
- Anticipated future behavior
- Patient opinion
- Undisclosed risk behaviors
  - Not everyone is comfortable disclosing every risk behavior

# HIV Prevalence in DC



More than 13,300 people live with HIV in the District of Columbia.



(HAHSTA 2016)

# Prescribing PrEP



# Prescribing PrEP



## Truvada

(Emtricitabine/tenofovir  
disoproxil fumarate)

1 pill daily

- Write first prescription for 30 days
- Refills: no more than 90 days

# Time to achieving protection

- From pharmacokinetic studies of TDF in HIV-negative men and women, time to protective effects varies by tissue.



- “There is not scientific consensus on what intracellular concentrations are protective for either drug or the protective contribution of each drug in specific body tissues.” (CDC 2014)

# Baseline labs

- HIV testing: 4th generation HIV – ½ Ag/Ab
- Hepatitis B and C serologies
  - A patient with undiagnosed Hepatitis B can have a serious relapse if PrEP is started and stopped.
- STI testing
  - Syphilis
  - Gonorrhea/Chlamydia
    - Urethral
    - Oral and rectal cultures (recommended)



# Baseline labs

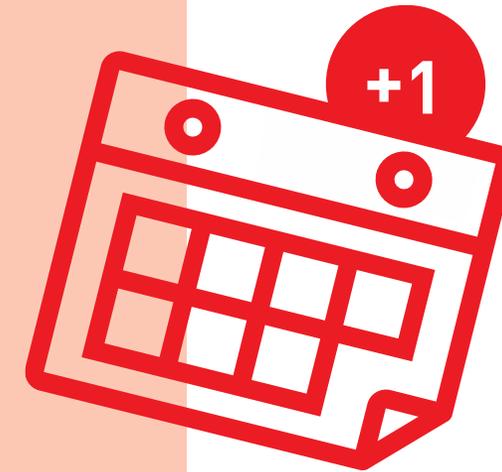
- Estimated creatinine clearance (eCrCl)  $\geq$  60 ml/min
- Metabolic profile
  - Kidney function
  - Blood count
- Immunization status
  - HPV



# Follow-up: 1 month after initiation

## ASSESS AND ADDRESS

- Signs or symptoms of acute HIV
- Adherence
- Adverse effects
- Sexual activity, condom use, and substance use
- Other issues or questions



# Follow-up: Ongoing



## EVERY 3 MONTHS

- Test for
  - HIV
  - STIs
  - Pregnancy
- Assess adverse effects, adherence, and HIV acquisition behavior



## EVERY 6 MONTHS

- Monitor eCrCl
  - Monitor more frequently in patients at higher risk of kidney damage (hypertension, diabetes)

# Contraindications

1 Lactic acidosis/severe hepatomegaly with steatosis

3 People with creatinine clearance less than 60 mL/min

2 Hepatitis B infection

# Drug interactions

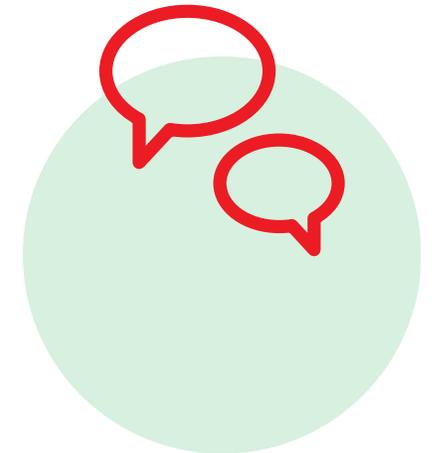
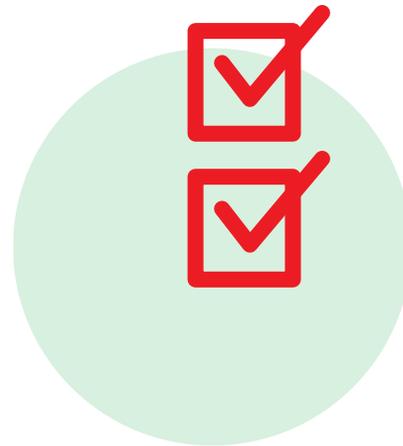
- Do not use with drugs affecting renal function.
- Do not use with drugs used to treat HIV.
- For patients taking other Hepatitis B meds, specialty consultation should be sought as some Hepatitis B drugs interact with PrEP.

(FDA 2012)



# Clinical Provider's Supplement

- Initiation Checklist
- Patient Information
- Counseling on Adherence



# Counseling patients about PrEP



- Complete sexual and substance use history
- Discussion of HIV prevention tools/strategies

# Reasons to offer PrEP



- Prevents HIV transmission in serodiscordant couples
- Fosters peace of mind
- Empowers receptive partner
- User-controlled and concealable
- Allows for conception
- Added protection as an adjunct to condoms
- Protects against HIV transmitted through sex or needles

# Bias against prescribing PrEP

## SEXUAL ORIENTATION

Not all patients will self-identify as gay or bisexual

## RACE

Black MSM are less likely to be prescribed PrEP

## GENDER

Women are less likely to be viewed as at risk

# PrEP Myths

## MYTH

PrEP protects against STIs (chlamydia, syphilis, gonorrhea, Hepatitis C)

## FACT

PrEP only protects against HIV. STIs are on the rise! Only condoms protect against other STIs

## MYTH

PrEP protects against pregnancy

## FACT

PrEP allows pregnancy

## MYTH

PrEP is a lifetime commitment

## FACT

Level of risk for HIV changes. Seasonal use is ok

## MYTH

PrEP is for everyone!

## FACT

Patients with renal failure, bone loss, liver problems or who are taking multiple drugs should not use PREP

# Common myths

Only Infectious  
Disease specialists  
should prescribe  
PrEP

Patients will  
disclose all of  
their HIV risk  
factors

PrEP is  
only for  
gay men

PrEP will lead  
to increased  
risk behavior

# Perceived barriers to PrEP administration



Time for  
physicians to  
counsel patients



Cost and  
access



Determining  
eligibility

# Key Messages



- One pill every day
- PrEP is only effective when the pill is taken regularly
- PrEP is not 100% effective
  - Concurrent condom use maximizes protection
- Discuss common and severe side effects
- Follow-up labs are important

# Services and resources

OFFER EDUCATIONAL MATERIALS  
AND FREE CONDOMS TO PATIENTS

- Patient information materials available through CDC
- Free condoms available through DC Department of Health
- RubberRevolutionDC.com



Check your local  
health department  
website for  
services in your  
area

# Services and resources in the District of Columbia



Helping Individual Prostitutes to Survive (HIPS)



The Women's Collective



Unity Health Care



Sasha Bruce



Us Helping Us



Whitman-Walker Health



Metro Teen AIDS



HOYA Clinic



Blair Underwood Healthcare Clinic (AHF)



Andromeda

# DC Center for Rational Prescribing



To find more modules,  
visit [doh.dc.gov/dcrx](https://doh.dc.gov/dcrx)

# Other DCRx Modules



Myths and Facts about Opioids



Getting Patients Off of Opioids



Medical Cannabis: An Introduction to the Biochemistry & Pharmacology



Rational Prescribing in Older Adults



Medical Cannabis: Evidence on Efficacy



Drug Approval and Promotion in the United States



Medical Cannabis: Adverse Effects and Drug Interactions



Generic Drugs: Myths and Facts

More resources available at the DC Center for Rational Prescribing

[doh.dc.gov/dcrx](https://doh.dc.gov/dcrx)