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*Department of Medicine*

# Pre-Exposure Prophylaxis (PrEP) for the Prevention of HIV Infection

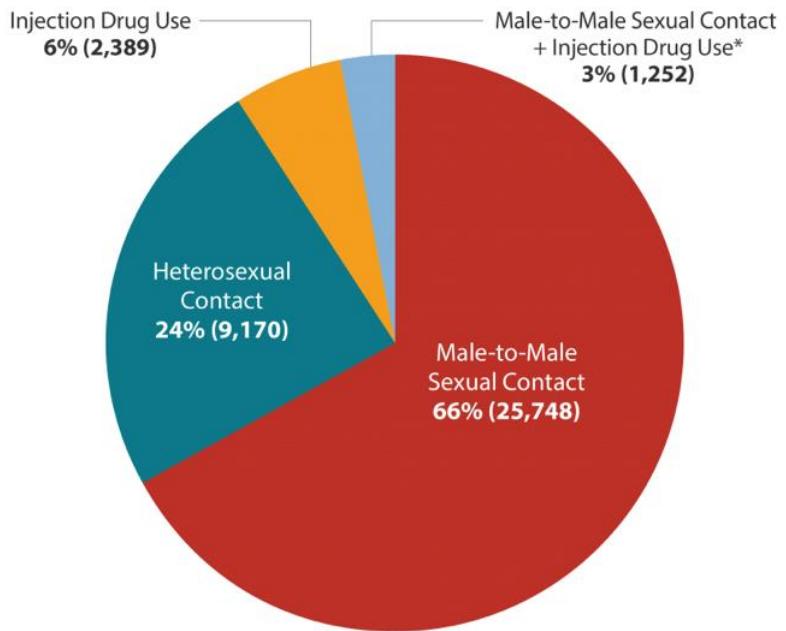
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# Epidemiology of HIV in the United States



- 1.1 million people in the U.S. are living with HIV
- 15 percent of people who are infected with HIV (1 in 7) are unaware they are infected
- **About 39 000 people get infected with HIV each year**
- In 2016 there were about 15 100 deaths (of any cause) among people with diagnosed HIV in the United States

New HIV Diagnoses in the United States and 6 Dependent Areas by Transmission Category, 2017



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

# Estimated Per-Act Probability of Acquiring HIV from an infected source, by Exposure Act



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Type of Exposure	Risk per 10 000 Exposures
<b>Parenteral</b>	
Blood transfusion	9250 (9/10)
Percutaneous (Needle Stick)	23 (1/423)
<b>Sex</b>	
Receptive Anal Intercourse	138 (1/72)
Insertive Anal Intercourse	11 (1/900)
Receptive Penile-Vaginal Intercourse	8 (1/1250)
Insertive Penile-Vaginal Intercourse	4 (1/2500)
Receptive Oral Intercourse	Low
<b>Other: Biting/Spitting</b>	Negligible

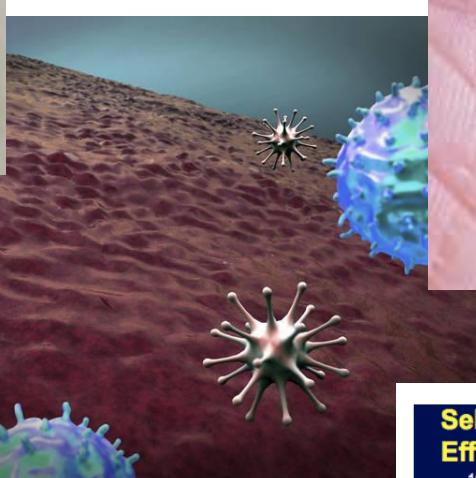
Patel P, Borkowf CB, Brooks JT. Et al. Estimating per-act HIV transmission risk: a systematic review. AIDS. 2014. doi: 10.1097/QAD.0000000000000298.

# PrEP Statistics

- 1.1 million individuals in the United States are at substantial risk for HIV and should be offered PrEP.
- The estimated number of U.S. PrEP users at the end of 2018 was 269 000.
- In 2017 only 67% of US Primary Care providers have heard of PrEP and only 11% have prescribed PrEP.



# Landmark PrEP Trials

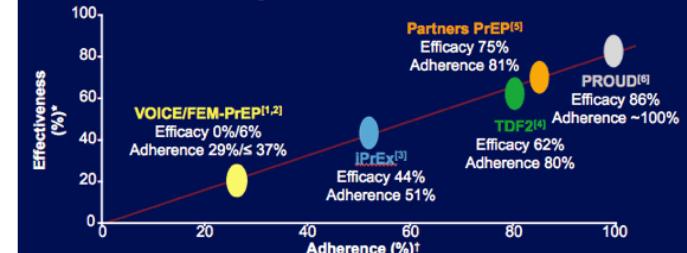


## Prep Efficacy Trials

Study Name	Population	N	Results	Efficacy Drug
Partners PrEP	Heterosexual couples	4,758	TDF: 67% efficacy FTC/TDF: 75% efficacy	86% 90%
TDF2 Study	Heterosexual Men and Women	1,219	FTC/TDF: 62% efficacy	85%
iPrEx	MSM/trans women	2,499	FTC/TDF: 44% efficacy	92%
FEM-PrEP	Women	1,951	FTC/TDF: futility	NR
VOICE	Women	5,029	TDF, TDF/FTC, Vaginal TFV gel: futility	NR
Thai IVDU	IVDU	2,413	TDF: 49% efficacy	74%

Kanke E, et al. 19th IAC, Washington, DC, May 22-27, 2012. Abstr TIAA0705.

## Select Daily Oral TDF/FTC PrEP Trials: Effectiveness Improves With Adherence



FTC, emtricitabine; PrEP, pre-exposure prophylaxis; TDF, tenofovir disoproxil fumarate.

# Landmark trial of antiretroviral Pre-exposure Prophylaxis among MSM



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## Pre-exposure Prophylaxis Initiative Trial (iPrEx)

Grant et al, N Engl J Med 2010;363:2587-2599

- Phase 3, randomized, double blind, placebo controlled international multi center trial.
- 2499 HIV sero-negative MSM randomized (between 2007 and 2009) to Placebo or FTC-TDF once daily.
- Followed for 1.2 to 2.8 years.
- The treatment group had a 44% risk reduction of being infected with HIV. Adherence to the study drug significantly increased the protective effect up to 92%.
- Side effect profile was benign with more nausea in the treatment group in the first month.

# Landmark trial of antiretroviral Pre-exposure Prophylaxis among heterosexual men and women



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## Partners PrEP Trial

Baeten JM et al, N Engl J Med 2012;367:399-410

- Phase 3 randomized, double blind, placebo controlled multicenter study in Uganda and Kenya
- 4758 HIV1- serodiscordant couples, 1/3 assigned to placebo, 1/3 assigned to TDF and 1/3 assigned to TDF/FTC.
- Followed for 36 months
- Relative risk reduction of 67% in the incidence of HIV1 with TDF and 75% with TDF/FTC.
- In patients with high medication adherence the relative risk reduction of HIV1 infection was 90%.
- There were no significant differences in serious adverse events between the groups

# Landmark trial of antiretroviral Pre-exposure Prophylaxis among Persons who inject Drugs



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## Bangkok Tenofovir Study

Choopanya K et al, Lancet 2013:381:2083-90

- Phase 3, randomized, double blind, placebo controlled study
- 2413 injection drug user in Bangkok, Thailand
- Followed for a mean of 4.6 years.
- There was a 49% reduction in risk of HIV acquisition among those receiving Tenofovir (33/1207 in Placebo group, 17/1204 in Tenofovir group)
- In patients with high adherence to the trial medication, the risk reduction of developing HIV was 73.5%

## Clinical case

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J. V. is a 24 year old man who presents to your clinic to establish Primary Care.

He is very interested in being tested for STIs.

How do you evaluate him?

# Identifying Indications for PrEP



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- Take a thorough sexual history in everyone e.g. : *"In the past 6 months have you had sex with men, women or both?"* Then ask about anal sex, receptive sex, condom use, HIV status of partners.
- Screen for alcohol abuse
- Screen for other substance abuse



## Clinical case

J. V. tells you that after breaking up with his long term boyfriend 5 months ago, he has had sexual intercourse with three different men.

He did have receptive anal intercourse without using a condom once or twice.

He does not know the HIV status of his partners.

He drinks about 3 beers per week and does not use any illegal substances

# MSM risk index

**1. How old are you today?**

If <18 years, score 0.  
 If 18-28 years, score 8.  
 If 29-40 years, score 5.  
 If 41-48 years, score 2.  
 If 49 years or more, score 0.

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**2. In the last 6 months, how many men have you had sex with?**

If >10 male partners, score 7. If 6–10 male partners, score 4. If 0-5 male partners, score 0.

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**3. In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom?**

If 1 or more times, score 10.  
 If 0 times, score 0.

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**4. In the last 6 months, how many of your male sex partners were HIV-positive?**

If >1 positive partner, score 8 If 1 positive partner, score 4. If <1 positive partner, score 0.

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**5. In the last 6 months, how many times did you have insertive anal sex (you were the top) without a condom with a man who was HIV- positive?**

If 5 or more times, score 6.  
 If 0 times, score 0.

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**6. In the last 6 months, have you used methamphetamines such as crystal or speed?**

If yes, score 6 If no, score 0.

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Add down entries in right column to calculate total score.

**TOTAL SCORE\***

\*If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.  
 If score is below 10, provide indicated standard HIV prevention services.

# Recommended Indications for PrEP Use by MSM



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- Adult man
- Without acute or established HIV infection
- Any male sex partners in the past 6 months
- Not in a monogamous relationship with a recently tested, HIV negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in the past 6 months
- A bacterial STI (Syphilis, Gonorrhea or Chlamydia) diagnosed or reported in the past 6 months

# Recommended Indications for PrEP Use by Heterosexually active Men and Women



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- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in the past 6 months
- Not in a monogamous relationship with a recently tested, HIV negative man

AND at least one of the following

- Is a man who has sex with both men and women
- Infrequent use of condoms with a partner of unknown HIV status who is known to be at substantial risk for HIV infection
- A bacterial STI (Syphilis, Gonorrhea or Chlamydia) diagnosed or reported in the past 6 months
- Is in an ongoing relationship with an HIV- positive partner

# Recommended Indications for PrEP Use by Persons who inject Drugs



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- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in the past 6 months

AND at least one of the following

- Any sharing of injection drugs or drug preparation equipment in the past 6 months
- Risk of sexual acquisition

## Clinical case

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You discuss PrEP with J.V. and he is very interested in starting to take this medication to prevent HIV infection.

What further evaluation you need to do prior to starting PrEP?

# Laboratory testing before starting PrEP

## HIV

- Clinicians should document a negative antibody test result within the week before initiating PrEP medications.
- Clinicians cannot accept patient-reported test results.
- Approved tests: Serum antigen/antibody test (highest sensitivity for acute HIV infection), Serum antibody-only test, FDA-approved fingerstick blood test
- Also: evaluate all patients for a history of nonspecific signs and symptoms of a viral infection

# Laboratory testing before starting PrEP

## Renal function

- Creatinine Clearance

Any person with a Creatinine Clearance of <60ml/min should not be prescribed PrEP.

## Hepatitis Serology

- Hepatitis B screening serology

Patients susceptible to HBV infection should be vaccinated

Patients who are HBsAg positive should be evaluated for treatment

- Hepatitis C

## Sexually transmitted diseases

Syphilis

Gonorrhea

Chlamydia (for sexually active MSM)

In MSM pharyngeal, rectal and urine specimens to test for Gonorrhea and Chlamydia should be collected.

## Clinical case

J.V. tests negative for HIV and Hepatitis C. He is immune to Hepatitis B. His renal function is within normal limits and he does not have G/C or Syphilis.

He is eager to start PrEP.

How do you prescribe the medication? How do you counsel the patient about side effects and adherence?

# Medications used for PrEP

Generic Name	Trade Name	Dose	Frequency	Common Side Effects
Tenofovir disoproxil fumarate (TDF)	Viread	300mg	Once per day	Nausea, Flatulence
Emtricitabine (FTC) (not recommended alone, only for use in combination with TDF)	Emtriva	200mg	Once per day	Rash, Headache
TDF + FTC	Truvada	300mg/200mg	Once per day	As above

## Efficacy of Truvada

99% for 7 doses/week, 96% for 4 doses/week, 76% for 2 doses/week

## Time to clinical effectiveness

Receptive anal sex → 7 days, receptive vaginal sex, IVDU → 20 days

# Clinical Follow up and Monitoring

Patients should return about every 3 months after PrEP initiation  
(Do not prescribe more than 90 days of PrEP)

To do list every 3 months

- Repeat HIV testing
- Repeat Pregnancy test for women who may become pregnant
- Provide a prescription refill for Truvada for no more than 90 days
- Assess side effects, adherence, and HIV acquisition risk behaviors
- Provide support for medication adherence

To do list every 6 months

- Monitor Creatinine Clearance
- Conduct STI testing

# Counseling for Medication Adherence



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- Understand what the patient knows about PrEP and why they are considering taking it.
- Explain in detail how to take the medication (e.g. when to take it, how many pills to take, what to do if a dose is missed, side effects)
- Explain that patients need to be tested for HIV every 3 months
- Discuss techniques to increase adherence



# Billing and Coding

While ICD-10 does not have specific codes for PrEP, the following codes can be used for PrEP visits:

- Z20.6 “Contact with and (suspected) exposure to HIV”
- Z17.1 “Human immunodeficiency virus (HIV) counseling
- Z11.3 “Encounter for screening for infection with a predominantly sexual mode of transmission”
- Z79 “Long-term (current) drug therapy, Includes long term (current) drug use for prophylactic purposes”

## Insurance questions

Please see handout

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# Questions?

# Time to positivity of HIV diagnostic tests

Test	Target of detection	Approximate time to positivity (days)
<b>Enzyme-linked Immunoassay</b>		
First generation	IgG antibody	35-45
Second generation	IgG antibody	25-35
Third generation	IgM and IgG antibody	20-30
Fourth generation	IgM and IgG antibody and p24 antigen	15-20
<b>Western blot</b>		
	IgM and IgG antibody	45-60
<b>HIV viral load test</b>		
Sensitivity cutoff 50 copies/ml	RNA	10-15
Sensitivity cutoff 1-5 copies/ml	RNA	5

# Alternatives to daily oral therapy

## Vacation therapy

(Patient knows that there will be a discreet period of time when high risk behavior will occur.)

Start taking daily PrEP 21 days (for women) or 7 days (for MSM) prior to high risk weeks. Continue daily PrEP for one month after.

## On demand PrEP

Take a loading dose (2 tablets of Truvada) 2-24 hours prior to sexual encounter.

Take one tablet daily while sexually active and continue for two more days post sexual activity

(Not FDA approved, but approved in some European countries (e.g. France)