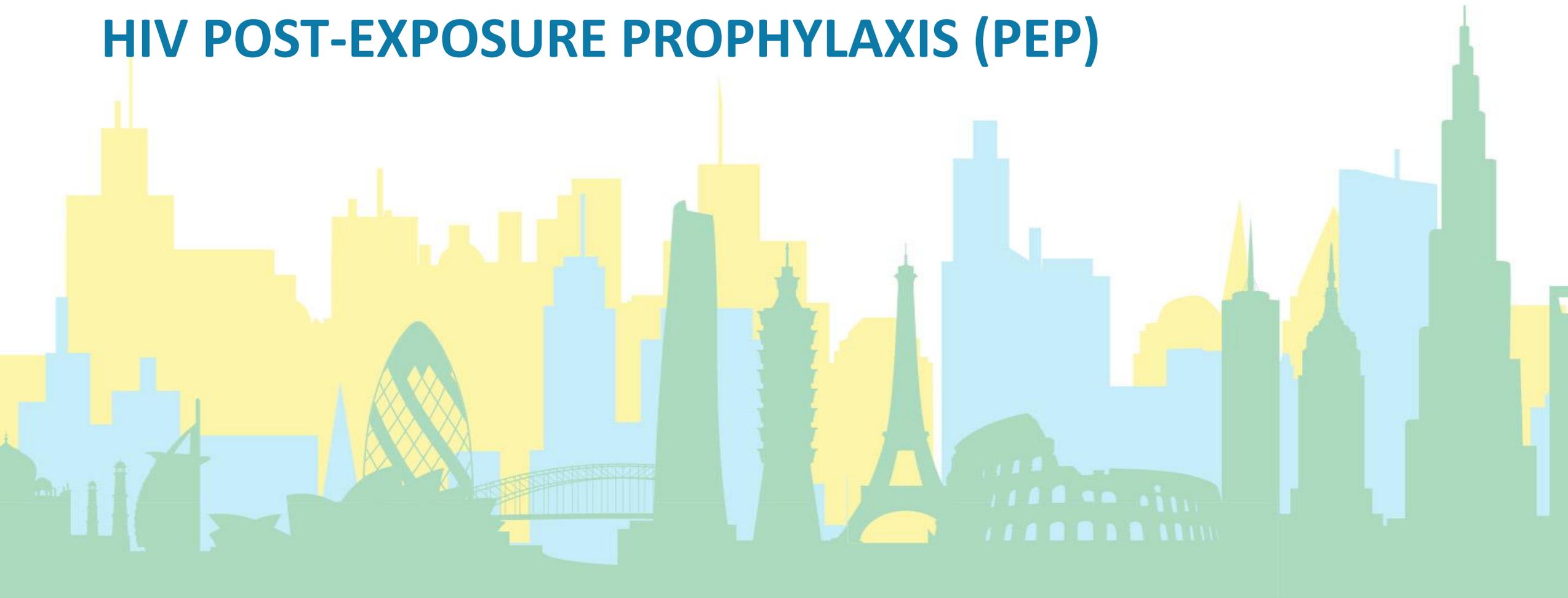


HIV PRE-EXPOSURE PROPHYLAXIS (PrEP)

HIV POST-EXPOSURE PROPHYLAXIS (PEP)



HIV Pre-Exposure Prophylaxis (PrEP) and HIV Post-Exposure Prophylaxis (PEP)

Intended Audience

Providers of HIV care in resource limited settings including, clinicians, clinical officers, nurses, pharmacists

AIMS

Build capacity to provide quality, accessible PrEP and PEP services to people at risk of acquiring HIV infection

LEARNING OBJECTIVES

The purpose of this module is to summarize

- Current WHO recommendations for provision of PrEP and PEP

After completing this module, you will be able to...

- Describe how PrEP and PEP are part of combination prevention
- Understand existing WHO recommendations for PrEP and PEP
- Describe who will benefit from PrEP and PEP

GOALS OF THE FAST-TRACK CITIES INITIATIVE



FAST-TRACK
CITIES

- Optimize the HIV care and prevention continua towards attainment of the global 90-90-90 targets
- Increase utilization of combination HIV prevention services
- Operationalize global and local treatment policies at the city clinic level
- Reduce to zero the negative impact of stigma and discrimination

SECTION 1

INTRODUCTION

COMBINATION PREVENTION

Biomedical, behavioral and structural interventions that decrease the risk of acquiring HIV

- **Structural**

- Policies
- Laws
- Regulatory environment
- Culture
- Cash transfers

- **Behavioral**

- Education
- Counselling
- Stigma reduction
- Harm reduction
- Adherence interventions

- **Biomedical**

- HIV testing
- Condoms
- VMMC
- PMTCT
- Treatment of STIs
- Antiretroviral therapy
- Pre-Exposure Prophylaxis (PrEP)
- Post-Exposure Prophylaxis (PEP)

This module examines PrEP and PEP



PrEP AND PEP DEFINITIONS

- **Pre-exposure prophylaxis (PrEP)** is the use of an antiretroviral medication to prevent the acquisition of HIV infection by uninfected persons
- **Post-exposure prophylaxis (PEP)** is short-term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse

Sources: (1) World Health Organization Guidelines on Postexposure Prophylaxis for HIV: Recommendations for a Public Health Approach. Ford N, Mayer K 2015
(2) Pre-exposure prophylaxis WHO <http://www.who.int/hiv/topics/pep/en/>

SECTION 2

Overview of PrEP

PrEP EFFICACY

In multiple studies^[1-6], oral tenofovir-based PrEP

- If taken correctly and consistently
- Reduces HIV infection risk
 - Heterosexual men and women
 - MSM
 - People who inject drugs



Numerous open label, demonstration and implementation projects have been conducted^[7]

1. Grant, R.M., et al., *Preexposure chemoprophylaxis for HIV prevention in men who have sex with men*. N Engl J Med, 2010. **363**(27): p. 2587-99.

2. Baeten, J.M., et al., *Antiretroviral prophylaxis for HIV prevention in heterosexual men and women*. N Engl J Med, 2012. **367**(5): p. 399-410.

3. Choopanya, K., et al., *Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study)*: Lancet, 2013. **381**(9883): p. 2083-90.

4. Thigpen, M.C., et al., *Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana*. N Engl J Med, 2012. **367**(5): p. 423-34.

5. Van Damme, L., et al., *Preexposure prophylaxis for HIV infection among African women*. N Engl J Med, 2012. **367**(5): p. 411-22.

6. Marrazzo, J.M., et al., *Tenofovir-based preexposure prophylaxis for HIV infection among African women*. N Engl J Med, 2015. **372**(6): p. 509-18.

7. AVAC, Ongoing and planned PrEP Demonstration and Implementation Studies. 2017.

PrEP ADHERENCE AND RETENTION



- Adherence to PrEP
 - Generally high in recent clinical implementation trials and demonstration projects [1-4]
 - Compared to earlier clinical trials where poor adherence was reported
- Retention rates in PrEP programs:
 - Have been suboptimal [5-6]
 - Discontinuation is common, up to 25% in some programs
- Restarts are also common as people cycle in and out of PrEP based on their assessment of risk

1. Koss, C.A., et al., *Differences in Exposure and Adherence to Tenofovir in the VOICE, iPrEx OLE, and PrEP Demo Studies as Determined via Hair Concentrations*. AIDS Res Hum Retroviruses, 2017.
2. Hoagland, B., et al., *the PrEP Brasil demonstration project*. J Int AIDS Soc, 2017. **20**(1): p. 21472.
3. Corneli, A.L., et al., *FEM-PrEP: adherence patterns and factors associated with adherence to a daily oral study product for pre-exposure prophylaxis*. J Acquir Immune Defic Syndr, 2014. **66**(3): p. 324-31.
4. Saag, M.S., *Preventing HIV in women--still trying to find their VOICE*. N Engl J Med, 2015. **372**(6): p. 564-6.
5. Underhill, K., et al., *Temporal Fluctuations in Behavior, Perceived HIV Risk, and Willingness to Use Pre-Exposure Prophylaxis (PrEP)*. Arch Sex Behav, 2018.
6. Whitfield, T.H.F., et al., *Why I Quit Pre-Exposure Prophylaxis (PrEP)? A Mixed-Method Study Exploring Reasons for PrEP Discontinuation and Potential Re-initiation Among Gay & Bisexual Men*. AIDS Behav, 2018.

KEY POPULATIONS AND PrEP

- Key populations up to 24 times more at risk of acquiring HIV ¹
 - Compared to adults in the general population
- Access to PrEP is a human right to health
- PrEP should be:
 - Made available, affordable, accessible
 - Offered in a manner appropriate to the needs of communities
- Community demand for PrEP is essential for enabling access
 - Especially where PrEP services are not widely available or not at all
 - Services must be offered in a way that meets the needs of PrEP users as this influences whether people actually choose to take PrEP

Source: The International Treatment Preparedness Coalition (ITPC) Key Population Activist Toolkit on PrEP

1. UNAIDS. Special analysis, 2016; Baral SD, Poteat T, Strömdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. *The Lancet Infectious Diseases*. 13(3): 214-222. March 2013.



ELIGIBILITY CRITERIA FOR PrEP

1

Confirmed HIV
negative

2

No signs or
symptoms of
acute HIV
infection

3

At substantial risk
of HIV infection

4

No
contraindications
to taking PrEP
medicines

5

Willingness to
use and adhere
to PrEP as
prescribed

- regular HIV testing

TESTING FOR HIV



- An HIV test is required to rule out infection prior to initiating PrEP
- Once a person has been initiated on PrEP, HIV testing is suggested:
 - Every three months
 - Whenever restarting PrEP after a gap
- Individuals with an inconclusive HIV test
 - Retested in 14 days

Sources: WHO Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO Module 10: For Testing Providers
Association of Inconclusive Sera for Human Immunodeficiency Virus Infection with Malaria and Epstein-Barr Virus Infection in Central Africa Francois-Xavier Mbopi-Keou, Angélique Ndjoi-Mbiguino, Frédéric Talla, Hélène Péré, Khady Kebe, Mathieu Matta, Maurice Aurelien Sosso, Laurent Bélec A. M. Caliendo, Editor DOI: 10.1128/JCM.02945-13

CONTRA- INDICATIONS FOR PREP



- HIV positive
- Signs or symptoms of acute HIV infection
- Recent exposure to HIV
- Estimated creatinine clearance of less than 60 ml/min (if known)
- Allergy or contraindication to any medicine in the PrEP regimen
 - Allergies to tenofovir, FTC or 3TC are uncommon

WHAT DO WE MEAN BY SUBSTANTIAL RISK OF INFECTION?

- HIV negative partner in a serodiscordant couple
 - Has a sexual partner with HIV who is not virally suppressed
- Vaginal or anal sex without a condom with more than one partner (including sex workers)
- Recent history in the past six months of an STI
- Use of PEP for sexual exposure in the past six months
- Use and/or inject drugs
- Requesting PrEP

SERO- DISCORDANT COUPLES



PrEP may be considered in the following situations

- HIV positive partner is not on antiretroviral therapy (ART)
- HIV positive partner has just started ART (within 6 months)
- HIV positive partner has sub-optimal adherence
- HIV negative partner
 - Has other partners besides the HIV positive partner on treatment

PEOPLE WHO USE AND/OR INJECT DRUGS

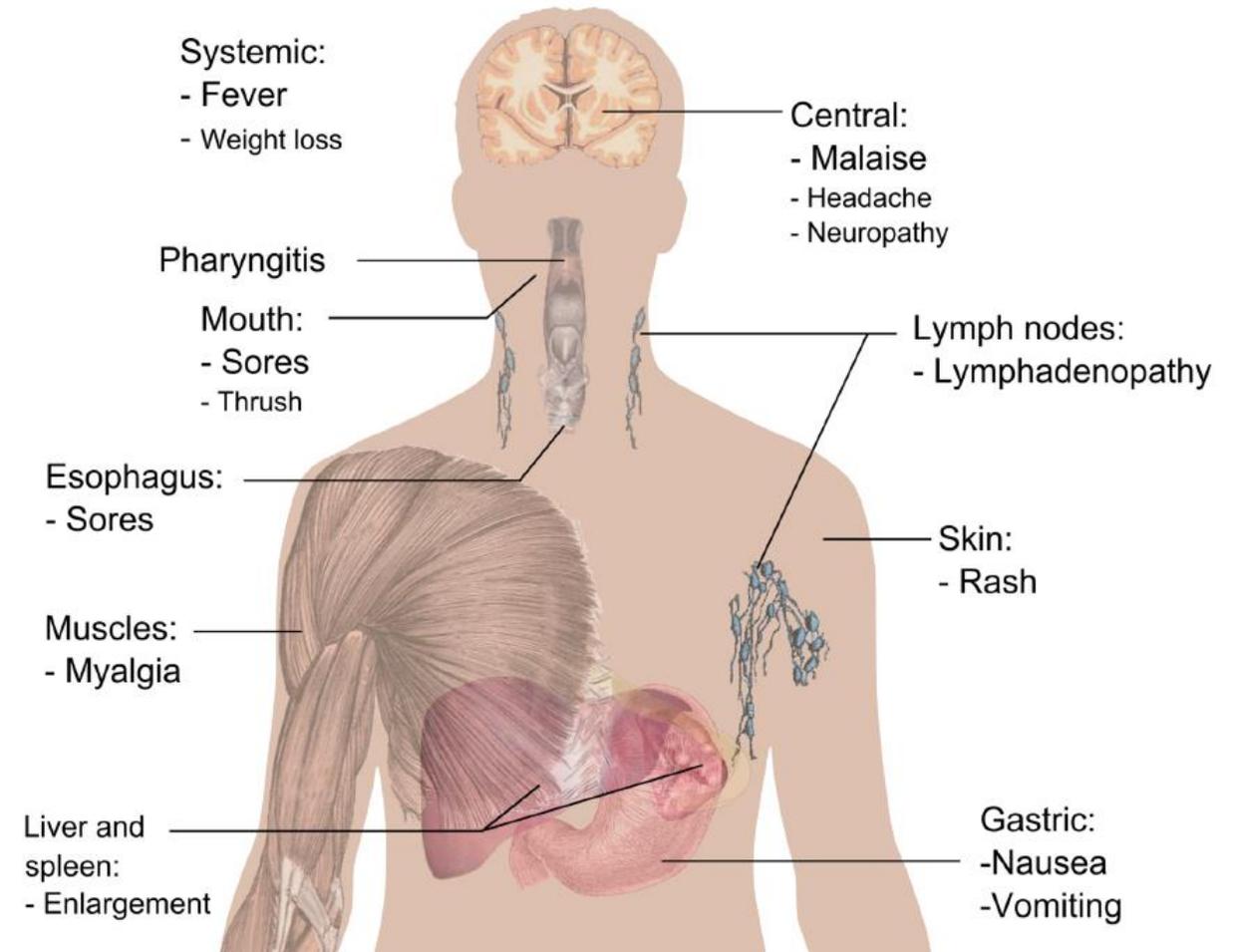


- People who use and/or inject drugs may be at substantial risk of acquiring HIV
- Access to harm reduction
 - Opioid substitution therapy and needle and syringe programs
 - Key HIV prevention intervention for people who inject drugs
 - Providing these services should be a priority
- People who use and/or inject drugs should not be excluded from PrEP

ACUTE HIV INFECTION

- Acute HIV infection (AHI) is the early phase of HIV disease
- AHI develops within 2-4 weeks after someone is infected with HIV
- 40-90% of people with AHI have flu-like symptoms
 - Not specific to HIV
 - Occur in many other viral infections
- Some people with AHI can be asymptomatic

Do NOT start PrEP in people with suspected AHI



GENERAL SCREENING QUESTIONS FOR PrEP

Any “yes” answer should prompt a discussion about PrEP

In the past 6 months...

Have you had sex with more than one person?

Have you had sex without a condom?

Have you had sex with anyone whose HIV status you do not know?

Have you injected drugs or shared injecting equipment?

Are any of your partners at risk of HIV?

Do you have sex with a person who has HIV?

MORE PrEP SCREENING QUESTIONS

Any “yes” answer may indicate increased vulnerability to HIV

Have you...

Started having sex with a new partner?

Received money, housing, food or gifts in exchange for sex?

Been forced to have sex against your will?

Used recreational or psychoactive drugs?

Been forced to leave your home because of violence or due to your sexual orientation or?

Lost a source of income and may need to exchange sex for housing, food or money?

Left school earlier than you planned?

ANTIRETROVIRAL DRUGS FOR PrEP

GENERIC NAME and ABBREVIATION	DOSAGE
Tenofovir disoproxil fumarate (TDF) + Emtricitabine (FTC)	Each tablet contains 300 mg of TDF and 200 mg of FTC
Tenofovir disoproxil fumarate (TDF) + Lamivudine (3TC)	Each tablet contains 300 mg of TDF and 300 mg of 3TC
Tenofovir disoproxil fumarate (TDF)	Each tablet contains 300 mg

NOTES ON SINGLE AGENT TENOFOVIR

WHO meta-analysis and the *Partners PrEP* trial

- TDF alone and TDF/FTC are comparably safe and effective
- Heterosexual men and women

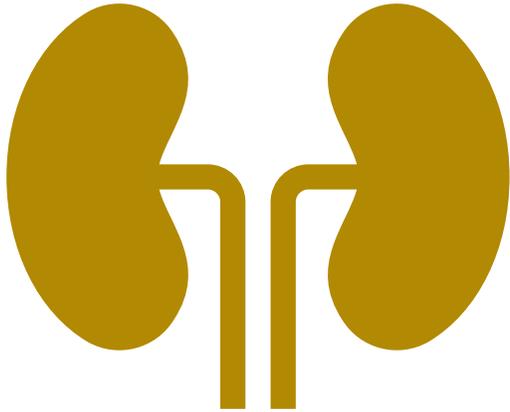
Limited evidence on the use of TDF alone for PrEP in MSM

- Cases have been reported of men acquiring HIV infection
- While taking TDF monotherapy for hepatitis B infection

Single agent TDF for PrEP may be considered ONLY

For the prevention of heterosexual HIV transmission

SIDE EFFECTS OF PrEP

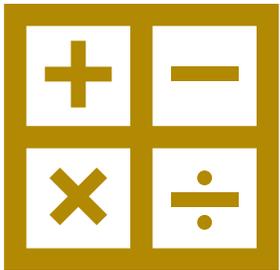


- PrEP is generally well tolerated
- 1 in 10 PrEP users may have side-effects including:
 - Nausea
 - Abdominal cramps
 - Headache
- Generally mild and resolve over the first month
- 1 in 200 may have creatinine elevation
 - Typically reversible if PrEP is stopped
- 1 in 100 may have loss of bone mineral density
 - Recovers after stopping PrEP
- Any decision to stop is on a case-by-case basis

DRUG INTERACTIONS

- Lamivudine (3TC) and emtricitabine (FTC) should not be used together
- TDF, FTC and 3TC have no known interactions with
 - Contraceptives
 - Hormones used for feminization by transgender women
 - Hormones used for masculinization by transgender men
 - Commonly used drugs
 - For tuberculosis or malaria
- No known interactions between PrEP drugs and alcohol or recreational drugs
- Detailed drug–drug interactions at <http://www.hiv-druginteractions.org>

TESTS WHILE TAKING PrEP



INITIAL TESTS

Suggested by WHO

- HIV testing (mandatory)
- Serum creatinine
- HBsAg
- Screening for STIs
 - Syphilis, gonorrhea, chlamydia
- Consider HCV testing for MSM

FOLLOW UP TESTS

Suggested by WHO

- Repeat HIV testing and STI screening (every 3 months)
- Serum creatinine (every 6 months)

Inability to perform the suggested tests should not be a reason for withholding PrEP in someone who is at substantial risk of HIV infection.

ESTIMATED CREATININE CLEARANCE

- Purpose is to monitor the potential renal toxicity of tenofovir in some people
- Use the Cockcroft–Gault Equation

$$\text{Estimated Cr Cl (mL/min)} = (1 \text{ for male, } 0.85 \text{ for female}) \times \frac{(140 - \text{age}) \times \text{Weight (kg)}}{\text{Serum Creatinine (mg / dL)} \times 72}$$

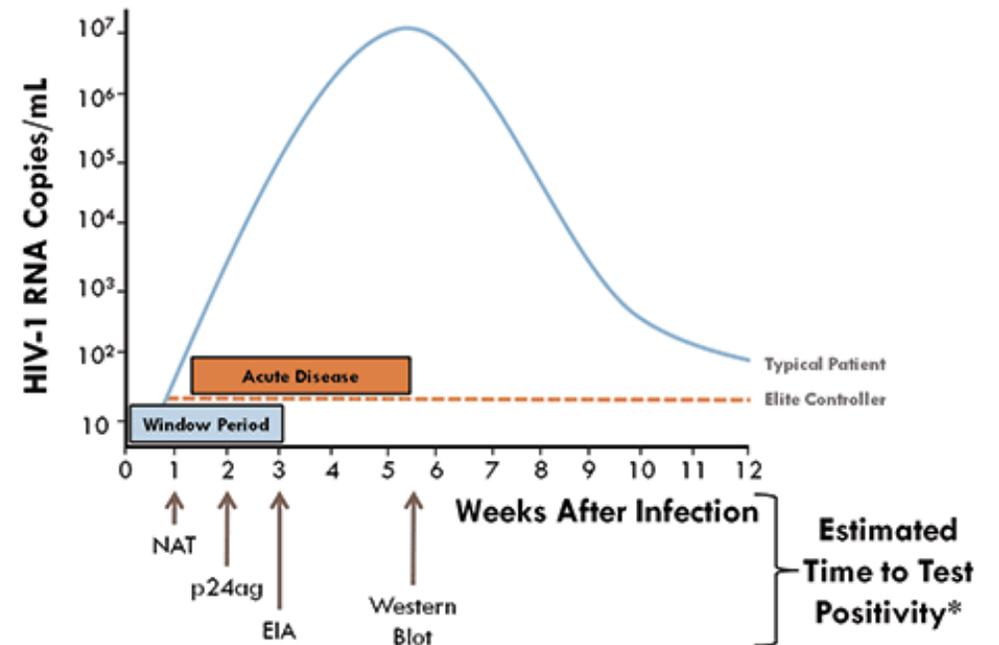
- Online calculators are available to make this calculation
- Estimated creatinine clearance of less than 60 ml/min is a contraindication for PrEP
- If Cockcroft-Gault calculation is not feasible
 - Consider excluding people with serum creatinine levels greater the upper limit of normal

CREATININE AND ESTIMATED CREATININE CLEARANCE

- WHO states that
 - “Whether monitoring renal function is essential to assure safe use of PrEP is not yet known”
- WHO **suggests** creatinine be measured
 - Before beginning PrEP
 - Every six months after the start of PrEP
- More frequent creatinine monitoring
 - Conditions that can affect renal function (diabetes or uncontrolled hypertension)
 - Optimal rate of more frequent monitoring is unknown
- Clinically significant creatinine elevations are rare in people:
 - Less than 45 years of age
 - Baseline estimated creatinine clearance more than 90 ml/min
 - Weigh more than 55 kg

MANAGEMENT OF SEROCONVERSION

- If a person using PrEP tests positive for HIV:
 - PrEP should be immediately discontinued
 - Antiretroviral triple therapy for HIV infection should be started without a gap after PrEP is discontinued
- WHO recommends:
 - Confirming reactive rapid test results by retesting a second sample according to the national testing algorithm before stopping PrEP and starting HIV treatment



*Schematic only, time to test positivity varies by patient

HANDLING AND STORAGE

- TDF, TDF/FTC and TDF/3TC are stored
 - Ambient room temperatures
 - 15–30 °C (59–86 °F)
- Avoid storage in hot (e.g., car) or cold places (e.g., refrigerator)
- Keep PrEP in its original container
 - With the drying agent
- PrEP users may transfer a supply to a pill box
 - For travelling
 - Help them to remember to take the medication daily

ADVICE FOR PrEP USERS

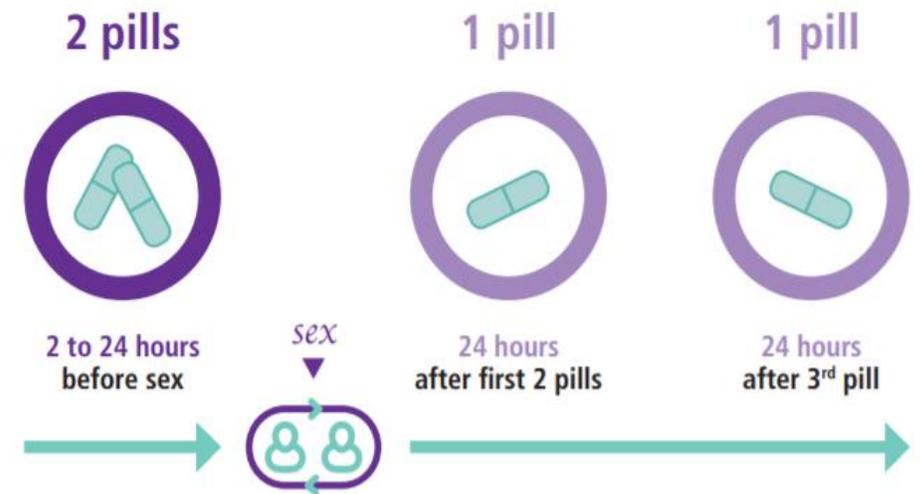


- Take one tablet each day
- PrEP does not protect against other sexually transmitted infections or prevent pregnancy
- Time is needed to build up protective levels
 - Additional HIV prevention should be taken for the first seven days of PrEP use
- If a PrEP dose is missed on a given day but realized the same day take as soon as remembered
- If not remembered until the next day, no need to take two pills on the same day
 - Take one tablet each day as usual

Event Driven PrEP (ED-PrEP)

July 2019
Update

- Taking PrEP medicines for a short period of time before and after HIV risk exposure, rather than every day
- WHO updated PrEP guidelines in July 2019
- Recommend Event Driven PrEP (ED-PrEP)
- **ONLY for MSM**
- “2+1+1” dosing



SPECIAL SITUATIONS

Situation	WHO recommendation
Hormonal contraception	PrEP does not alter the efficacy of hormonal contraceptives and hormonal contraceptives do not alter the effectiveness of PrEP
Pregnancy	PrEP may be offered or continued during pregnancy or breast feeding in women at substantial risk of HIV acquisition
Breast feeding	
Hepatitis B infection	Hepatitis B vaccination is appropriate PrEP can be provided whether or not HBV vaccination is available When PrEP is stopped, HBV infection can flare in the following 1-3 months ¹

1. The Safety of Tenofovir–Emtricitabine for HIV Pre-Exposure Prophylaxis (PrEP) in Individuals With Active Hepatitis B. Marc M. Solomon et al for the iPrEx Study Team J Acquir Immune Defic Syndr. 2016 Mar 1; 71(3): 281–286.

PrEP AND SEASONS OF RISK

- People often move in and out of seasons of risk (risky situations)
- People will not need to take PrEP all their lives
- Learning how to start and stop PrEP is key to effective use
- PrEP counseling creates an opportunity:
 - To recognize situations of possible HIV exposure use appropriate prevention strategies (e.g. PrEP)
 - To educate PrEP users on when the 'season of risk' passes and PrEP may be interrupted
- **NOTE:**
 - PrEP takes at least 7 days to reach protective levels
 - PrEP should be continued for 48 hours (2 doses) after the most recent risk exposure

Some reasons to consider starting PrEP

Planned sex without a condom

Alcohol and recreational drug use

Leaving a long-term relationship

Starting a relationship with a person with HIV who is not virally suppressed or on ART

Now we'll take a moment to review a case study about Charlotte, which illustrates how to start and stop PrEP in the real world



Charlotte is 18 years of age and has just left school

She met David at the market and they have been dating

They want to start having sex but decided to take an HIV test first

Charlotte's test was negative but David's test was positive

He has started antiretroviral therapy with tenofovir, 3TC and efavirenz

David is putting pressure on Charlotte to start having sex

David told Charlotte that he does not like to use condoms

Charlotte comes to your clinic for advice

How will you counsel her?



Charlotte is at substantial risk of acquiring HIV because...

- She is in serodiscordant relationship
 - She is HIV negative and David has just been diagnosed HIV positive
 - He has started ART but is not yet virally suppressed

Your counselling with Charlotte should include the following...

- Consistent and correct use of condoms will help protect Charlotte from getting HIV from David
- The couple should use condoms every time they have sex



Case Study (continued):

- Whether the couple consistently uses condoms or not, taking PrEP would give Charlotte additional protection
- But she must take it everyday
 - Until David has an undetectable viral load
 - Up to 6 months
- Taking prep will not protect Charlotte from other sexually transmitted diseases or from becoming pregnant
- Charlotte decides that she will start PrEP
- You test her for HIV again and she is negative
- You give Charlotte one month's supply of TDF/3TC



Case Study (continued):

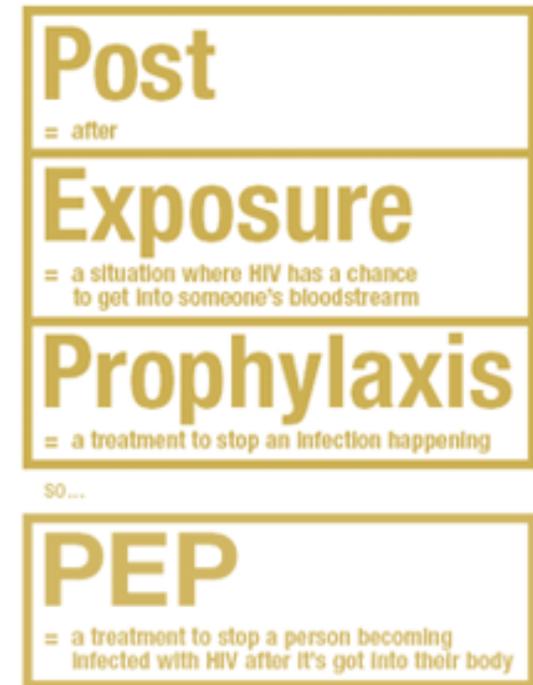
- You see Charlotte and David one month later
 - She never missed any doses of PrEP
 - David has not missed any doses of his HIV treatment
- You provide adherence counselling for both of them
 - Give Charlotte another three months of PrEP
- When the couple returns in 3 months
 - David shows you his viral load test which is undetectable
 - You advise Charlotte that she may now stop PrEP
 - Provide further adherence counseling for David

SECTION 3

Overview of PEP

What is PEP?

- PEP
 - Post-exposure prophylaxis
 - Following a possible exposure to HIV
- PEP may be offered following:
 - **Occupational**
 - HIV exposure while working
 - E.g., needlestick injury
 - **Non-occupational** exposure to HIV
 - HIV exposure from sex or injection drug use or other possible environmental exposures (e.g. stepping on a needle)
- PEP is for emergency situations, not for regular use



HIV POST EXPOSURE PROPHYLAXIS (PEP)

- PEP should be offered as soon as possible after exposure
 - Within 72 hours
- If possible exposure is more than 72 hours
 - PEP should not be offered
- Continued for 28 days and then stopped
- If seroconversion occurs while taking PEP
 - Triple ART should be continued without a gap

Post

= after

Exposure

= a situation where HIV has a chance to get into someone's bloodstream

Prophylaxis

= a treatment to stop an infection happening

so...

PEP

= a treatment to stop a person becoming infected with HIV after it's got into their body

EXPOSURE ASSESSMENT

Exposures that may warrant HIV PEP include:

- Bodily fluids: blood, blood-stained saliva, breast milk, genital secretions, cerebrospinal, amniotic, peritoneal, synovial, pericardial, or pleural fluids
- Mucous membrane: sexual exposure; splashes to eye, nose, or oral cavity
- Parenteral exposures: needlestick injuries



Exposures that do not require HIV PEP include when:

- The exposed individual is HIV already positive
- The source is established to be HIV negative
- Exposures to bodily fluids that do not pose a significant risk, such as tears, non-blood-stained saliva, urine or sweat

WHO SHOULD CONSIDER TAKING PEP?

???

- PEP is for people who are HIV negative or who do not know their HIV status
- In the last 72 hours:
 - Think they were exposed to HIV during work (e.g., needlestick injury)
 - Possibly exposed to HIV during sex
 - Were sexually assaulted
 - Shared needles or drug preparation equipment

PEP MEDICATIONS

1

TDF + 3TC (or FTC) is recommended

- Preferred backbone regimen
- PEP for adults and adolescents

2

Dolutegravir (DTG) is recommended as the preferred third drug

(Next screen outlines caveats on use in females)

3

When available, ATV/r, DRV/r, LPV/r and RAL may be considered as third drug options

Sources:

World Health Organization Guidelines on Postexposure Prophylaxis for HIV: Recommendations for a Public Health Approach. Ford N, Mayer K 2015

Updated Recommendations on First-Line and Second-Line Antiretroviral Regimens and Post-Exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV July 2018

PEP IN WOMEN AND ADOLESCENT GIRLS



- Dolutegravir can be prescribed
 - Women and adolescent girls of childbearing age or potential
 - Wish to become pregnant
 - OR who are not using consistent contraception
- **If** fully informed of the potential increase in the risk of neural tube defects at conception and until the end of the first trimester
- Offered pregnancy testing at PEP initiation and during follow-up on PEP
- Emergency contraception should be offered as soon as possible and within five days of the sexual exposure
- Information should be provided on the risks and benefits of DTG
- For women and adolescent girls who require PEP and who do not want to take emergency contraception or DTG, an alternative third ARV drug should be provided

TWO DRUG PEP REGIMENS



- Situations where only 2-drug regimens are available for PEP or where the risk of additional toxicity outweighs the benefit
- In these case, 2-drug regimens are acceptable
 - Supported by evidence from animal studies with PEP
 - Other ARV-based prevention interventions
 - Prevention of mother-to-child transmission (PMTCT)
 - Pre-exposure prophylaxis (PrEP)

SECTION 4

Conclusion

TRANSITION FROM PEP TO PrEP



- After 28 days of PEP, PrEP can be started
 - If the HIV test remains negative
 - AND there is substantial ongoing risk of HIV acquisition
- There should be no gap between finishing PEP and starting PrEP

Reflection Points

Let's reflect upon the content of this module:



Can you answer these questions?

- What is the difference between PrEP and PEP?
- Who is eligible for PrEP?
- What do we mean by “at substantial risk of acquiring HIV infection”?
- What blood tests are mandatory before starting PrEP?
- When should PEP be started & for how long should it be continued?
- What are the WHO recommended antiretrovirals for PEP?