



PRE-EXPOSURE PROPHYLAXIS (PREP) TRAINING FOR PROVIDERS IN CLINICAL SETTINGS

Participant Manual (Version 2.0)
2017



ICAP
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Mailman School of Public Health

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The *Pre-exposure Prophylaxis (PrEP) Training for Providers in Clinical Settings* was developed by ICAP at Columbia University in collaboration with the Centers for Disease Control and Prevention, with funding from PEPFAR. The training was developed as a set of tools that are adaptable to each county's local context and guidelines. The use of PrEP is an evolving area and it is therefore expected that these documents will require updating over time as recommendations change.

Organizations and entities that choose to adapt these documents for their own use should credit ICAP at Columbia University and note that their work is an adaptation.

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Foreword

Despite remarkable progress in HIV treatment, there were still an estimated 2.1 million new HIV infections globally in 2015. Thus, a large number of individuals remain at substantial risk for acquisition of HIV infection. Key populations at substantial risk include sex workers (SW), men who have sex with men (MSM), transgender persons (TG), and people who inject drugs (PWID), as well as other priority populations such as young women in southern Africa. These realities compel the need for continued efforts to expand access to effective HIV prevention interventions while at the same time continuing the scale-up of access to HIV treatment programs for individuals living with HIV.

Pre-Exposure prophylaxis (PrEP) is a new, efficacious HIV prevention intervention. It involves the use of antiretroviral drugs (ARVs) by HIV un-infected persons to prevent acquisition of HIV. Several clinical trials have demonstrated the efficacy of PrEP in MSM and transgender women, serodiscordant couples, heterosexual men and women, and PWIDs. The efficacy of PrEP has varied widely across trials, largely based on the level of adherence achieved with the daily doses of tenofovir/emtricitabine (TDF–FTC). ‘Real world’ effectiveness of PrEP, particularly given concerns about adherence and risk compensation, was demonstrated in the PROUD study and also in several demonstration projects. Ultimately, PrEP works when it is taken as prescribed.

It is important to note that across all clinical trials and demonstration projects, PrEP was provided as a component of a package of HIV prevention interventions, including repeat HIV testing, promotion and provision of condoms, screening and management of sexually transmitted infections (STIs), adherence support, risk-reduction counseling, and harm reduction interventions. Thus, there is global consensus that PrEP is an important tool in the package and that it should be offered to people at substantial risk of HIV infection as part of a combination HIV prevention approach.

This training manual for PrEP implementation was developed specifically for the use of PrEP for health workers in clinical settings. The goal is to enable clinical providers to attain the skills required to provide PrEP to appropriate candidates in an effective and safe manner. The training provides information regarding the evidence for PrEP effectiveness, PrEP procedures, and monitoring. It also includes a set of job aids. It is anticipated that facilities will need to adapt this training material to reflect specific contexts and include evidence from new research and experience in the use of PrEP.

PrEP offers a unique opportunity to confront the HIV epidemic, prevent HIV acquisition by individuals at risk for HIV, and reach global targets.

We welcome feedback regarding this training.

ICAP at Columbia University
New York, December 2016
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Acronyms

AHI	Acute HIV Infection
ART	Antiretroviral Therapy
ARV	Antiretroviral
CDC	US Centers for Disease Control and Prevention
FSW	Female Sex Worker
FTC	Emtricitabine
Ab/Ag	Antibody/Antigen
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HIV-DR	HIV Drug Resistance
HTS	HIV Testing Services <i>or</i> HIV Testing Strategy
iNSC	Integrated Next Step Counselling
MSM	Men who have Sex with Men
NSC	Next Step Counselling
PEP	Post-Exposure Prophylaxis
PMTCT	Preventing Mother To Child Transmission
PrEP	Pre-Exposure Prophylaxis
PWID	People Who Inject Drugs
RCT	Randomized Controlled Trial
RNA	Ribonucleic Acid
RPR	Rapid Plasma Regain test (syphilis)
STI	Sexually Transmitted Infection
TasP	Treatment as Prevention
TDF	Tenofovir Disoproxil Fumarate
UNAID	Joint United Nations Programme on HIV/AIDS
VMC	Voluntary Male Medical Circumcision
WHO	World Health Organization
3TC	Lamivudine

Training Overview

Training Goals and Development

The goal of the *Pre-exposure prophylaxis (PrEP) Training for Providers in Clinical Settings* is to equip HIV care providers with the knowledge and skills necessary to provide PrEP to appropriate candidates and with high quality in order to decrease the risk of HIV infection.

ICAP at Columbia University (ICAP) used a backward design approach to develop this training. First, content and training experts were identified. Together these experts developed a series of competency statements (tasks or skills) that HIV care providers would need in order to provide PrEP to appropriate candidates with the required level of proficiency. Next, the team created learning objectives and assessment measures to describe what HIV care providers should be able to achieve at the end of the training program. These learning objectives were then sequenced and grouped into six learning modules. Finally, the team created learning activities and training tools for all learning objectives. Training tools include a facilitator manual, participant manual, job aids, monitoring and evaluation tools, and a comprehensive slide set with essential content, visuals, and talking points.

Competencies and Content Areas

The core competencies health providers will develop during the training are:

- Identify eligible candidates for PrEP.
- Assess individual risk for HIV.
- Educate and counsel PrEP candidates and users.
- Assess medical eligibility for PrEP.
- Prescribe PrEP.
- Conduct clinical and laboratory assessments during follow-up PrEP visits.
- Assess PrEP Monitoring and Evaluation tools for local use.
- Provide adherence education, counseling and support to PrEP candidates and users.

This is a classroom-based training. Content areas are:

- PrEP basics
- PrEP screening and eligibility
- Initial and follow-up PrEP visits
- Monitoring and managing PrEP side effects, seroconversion, and stigma
- Monitoring and evaluation tools for local use

The target population for this training is providers with **existing** knowledge and experience in HIV prevention, care, and treatment, including:

- Physicians
- Medical officers
- Clinical officers
- Nurses
- Nurse midwives
- Prevention and treatment counselors

Participant Manual

This participant manual is divided into six modules, each containing the learning objectives, key technical content, scenarios, and role-play instructions. Participants will use this manual throughout the training. In some training sessions, participants will close their manuals in order to attend to an interactive trainer presentation. In other sessions, participants will have their manuals open in order to read content or follow activity instructions. Participants should take their manuals home after the end of the training so they can be used as reference.

PrEP Resources

PrEP Resources for Providers

- <http://www.who.int/hiv/pub/arv/arv-2016/en/>
- <http://www.who.int/hiv/topics/prep/en/>
- http://www.unaids.org/sites/default/files/media_asset/UNAIDS_JC2764_en.pdf
- <http://www.prepwatch.org/>
- <http://www.cdc.gov/hiv/risk/prep/>
- Glidden, DV, Amico, KR, Liu AY, et al. Symptoms, side effects and adherence in the iPrEx open-label extension. Clin Infect Dis. 2016;62(9):1172-7.
- Fonner, VA, Dalglish, SL, Kennedy, CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. AIDS 2016;30(12):1973-1983.
- The Fenway Institute. Pre-exposure prophylaxis clinical study data sheet. <http://www.projectinform.org/pdf/prepstudydata.pdf> . Accessed October 5, 2016.
- World Health Organization. Review: Safety of tenofovir PrEP in pregnant and breastfeeding HIV-uninfected women and their infants. <http://emtct-iatt.org/wp-content/uploads/2016/08/WHO-TDF-pregnancy-Lynne-Mofenson.August-21-2016.pdf> . Accessed October 5, 2016.

PrEP Resources for PrEP Users

- <http://www.whatisprep.org>
- <http://www.PleasePrEPMe.org/resources>
- <http://www.iwantprepnnow.co.uk>
- http://www.cdc.gov/hiv/pdf/risk_PrEP_TalkingtoDr_FINALcleared.pdf
- <https://www.facebook.com/groups/PrEPFacts/>

MODULE 1: PrEP Basics

OBJECTIVES

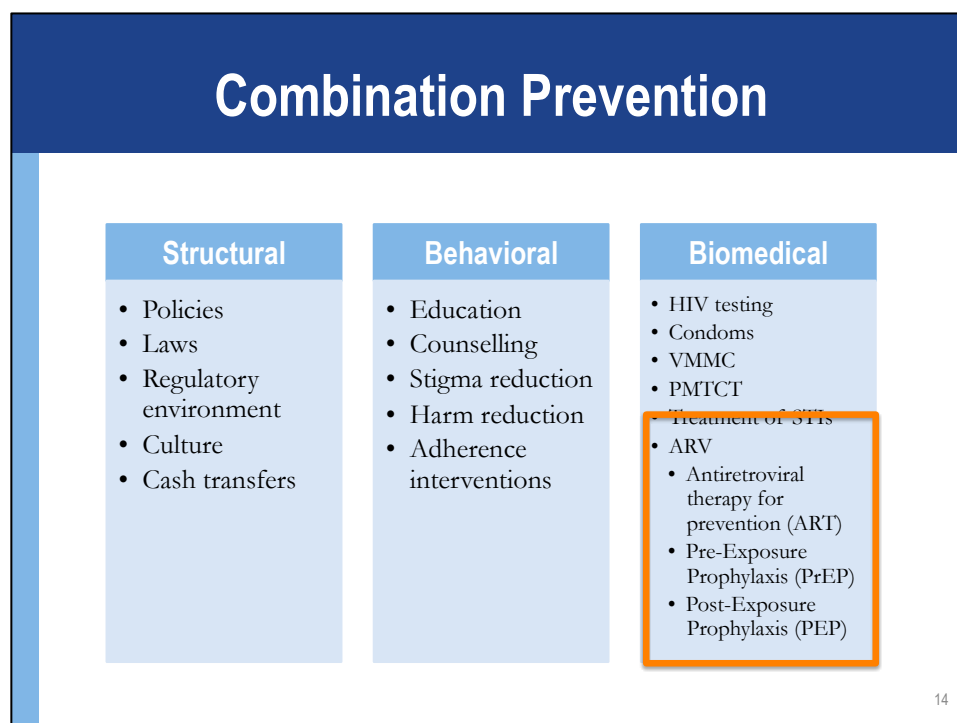
After completing Module 1, you will be able to:

- Define PrEP.
- Differentiate PrEP from PEP and ART.
- Describe the need for PrEP.
- Identify people at risk and people at substantial risk for HIV infection.
- Identify key populations (KP) for PrEP at the local level.
- Explain the relationship between PrEP effectiveness and adherence.
- State key reasons why PrEP is needed.
- Specify the PrEP regimens approved by WHO and within one's own country.
- Identify concerns regarding the implementation of PrEP.
- Explain the risks and benefits of PrEP.

INTRODUCTION

HIV prevention needs change during a person's lifetime.

Combination prevention is a mix of biomedical, behavioral, and structural interventions that decrease risk of HIV acquisition. Combining approaches may result in greater impact than using single interventions alone. Antiretroviral drugs (ARVs) used as PrEP provide an important **additional prevention tool**.



DEFINITIONS

Pre-exposure Prophylaxis (PrEP) is the use of ARV drugs by HIV-uninfected persons to prevent the acquisition of HIV before exposure to HIV.

- Pre = Before
- Exposure = Activity that can lead to HIV infection
- Prophylaxis = Prevention

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. Within the health sector, PEP should be provided as part of a comprehensive universal precautions package that reduces staff exposure to infectious hazards at work.¹

¹ <http://www.who.int/hiv/topics/prophylaxis/en/>

DIFFERENCES BETWEEN PrEP, PEP, and ART

PrEP and PEP

Comparing PrEP (*Pre-Exposure Prophylaxis*) and PEP (*Post-Exposure Prophylaxis*)

What's the same?

- Both are used by HIV uninfected persons
- Both use ARVs to prevent HIV acquisition
- Both are available from a clinical provider by prescription
- Both are effective when taken correctly and consistently

What's different?

- PrEP is started BEFORE potential exposure and PEP is taken AFTER exposure
- PEP is taken for 28 days only. PrEP requires ongoing use as long as HIV risk exists

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ART and PrEP

HIV treatment requires adherence to life-long therapy with consistent, fully suppressive dosing.

PrEP is needed during “*periods*” of high HIV risk.

- Both ART and PrEP require optimal adherence.
- Individuals taking PrEP require ongoing risk assessment and PrEP can be discontinued if individuals:
 - Acquire HIV infection.
 - Are no longer at substantial risk for HIV infection.
 - Decide to use other effective prevention methods.

Motivation for adherence is different: ART is taken by HIV-infected persons who may have symptoms to remain healthy and prevent onward transmission, while PrEP is taken by HIV uninfected persons who are largely healthy, to prevent acquisition of infection.

WHY WE NEED PrEP²

There are already several effective HIV prevention interventions (e.g. condoms, harm reduction for people who inject drugs (PWID)).

- However, globally there were more than 2 million new HIV infections in 2015.
- HIV incidence among key and vulnerable populations remains high (e.g. men who have sex with men (MSM), sex workers (SWs), PWIDS, transgender persons, etc.).

PrEP provides an *additional* prevention intervention to be used **together** with existing interventions (e.g. condoms).

PrEP is not meant to replace or be a substitute for existing interventions.

(The trainer will provide information on local epidemiology.)

PrEP STUDIES

ARVs Used in PrEP Trials

- **Oral daily tablet of TDF/FTC** (300mg tenofovir disoproxil fumarate/200mg emtricitabine)
- **Oral daily tablet of TDF** (300mg tenofovir disoproxil fumarate)
- PrEP using TDF/FTC and TDF alone are both equally safe and effective for heterosexual men and women.
- TDF alone was also found to be effective in PWIDs.
 - There is limited evidence on the use of TDF alone for PrEP in MSM.
- TDF/FTC was approved for PrEP by the Food and Drug Administration (FDA) in 2012.

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² UNAIDS, Gap Report 2016

iPrEx study



Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

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ABSTRACT

BACKGROUND: Antiretroviral chemoprophylaxis before exposure is a promising approach for the prevention of human immunodeficiency virus (HIV) acquisition.

METHODS: We randomly assigned 2499 HIV-seronegative men or transgender women who have sex with men to receive a combination of two oral antiretroviral drugs, emtricitabine and tenofovir disoproxil fumarate (FTC-TDF), or placebo once daily. All subjects received HIV testing, risk-reduction counseling, condoms, and management of sexually transmitted infections.

RESULTS: The study subjects were followed for 3324 person-years (median, 1.2 years; maximum, 2.8 years). Of these subjects, 10 were found to have been infected with HIV at enrollment, and 100 became infected during follow-up (16 in the FTC-TDF group and 84 in the placebo group), indicating a 44% reduction in the incidence of HIV (95% confidence interval, 15 to 65; $P=0.0005$). In the FTC-TDF group, the study drug was detected in 22 of 41 of seronegative subjects (54%) and in 3 of 34 HIV-infected subjects (9%) ($P<0.0001$). Nausea was reported more frequently during the first 4 weeks in the FTC-TDF group than in the placebo group ($P<0.0001$). The two groups had similar rates of serious adverse events ($P=0.57$).

CONCLUSIONS: The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Grant at the J. David Gladstone Institutes, University of California at San Francisco, 1650 Owens St., San Francisco, CA 94143, or at robert.grant@ucsf.edu.

*Other members of the Preexposure Prophylaxis Initiative (iPrEx) study team are listed in the Supplementary Appendix, available at NEJM.org.

This article (DOI:10.1056/NEJMoa1012057) was published on November 23, 2010, and updated on December 1, 2010, at NEJM.org.

N Engl J Med 2010;363:2587-96.
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• Study Design

- N = 2499 HIV-seronegative men (or transgender women)
- Sexual orientation: sex with men
- All received risk reduction counseling, condoms, & STI Rx

• Regimens

- TDF/FTC (*Truvada*): 1 pill PO daily
- Placebo: 1 pill PO daily

• Result

- 44 % reduction in incident HIV in the TDF/FTC arm

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PROUD: Immediate vs. Deferred PrEP in High-Risk MSM in a “Real World” Trial

- Randomized, open-label trial of daily oral TDF/FTC PrEP in MSM in 13 STI clinics in London:
 - Immediate (n = 267) vs. deferred for 12 months (n = 256)
 - Primary endpoint: HIV infection in first 12 months from enrolment
 - Results:
 - **Incident HIV infection:** 3 in immediate arm, 20 in deferred arm
 - Reduction 86%, 90% CI 64-96, $p=0.0001$
 - Number needed to treat for 1 year to prevent 1 infection: 13 (90% CI: 9-25)

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ANRS IPERGAY: On-Demand Oral PrEP in High-Risk MSM

- Randomized double-blind trial
- **Event-driven oral TDF/FTC (n = 199) vs. placebo (n = 201)**
 - 2 tablets taken 2-24 hours before sex
 - 1 tablet taken 24 hours after sex
 - 1 tablet taken 48 hours after first event-driven dose
 - **Primary endpoint:** HIV seroconversion
 - **Results:**
 - **86% reduction in risk** seen in PrEP arm (95% CI: 40 -98, $P = 0.002$)
 - Median of 16 pills taken per month in each arm
 - **Number needed to treat for 1 year to prevent 1 infection: 18**

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Partners PrEP Demonstration Project

- Open label multi-country study
- Integrated delivery of PrEP and ART in sero-discordant couples
- Sero-discordant couples:
 - Oral daily TDF/FTC given as PrEP to HIV-uninfected partner and continued six months beyond initiation of ART for infected partner
- Interim analysis:
 - **96%** reduction in expected infections (*all* HIV infections)

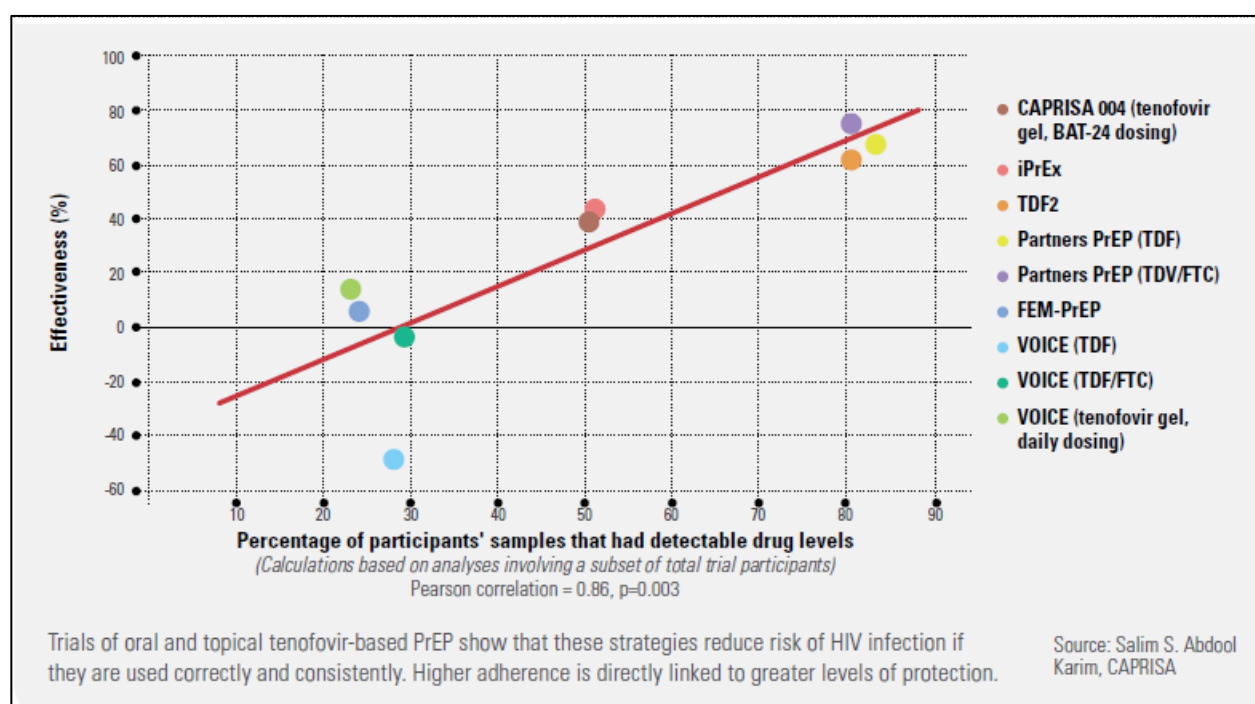
PrEP can be used as a 'bridge' to fully suppress ART in serodiscordant couples

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Key HIV PrEP Trials Using Oral Tenofovir (TDF) or Tenofovir-Emtricitabine (TDF-FTC)			
Study	Study Population	Study Randomization	HIV Incidence Impact
IPrEx (Brazil, Ecuador, South Africa, Thailand, US)	2499 MSM and transgender women	Daily oral TDF-FTC or placebo	TDF-FTC: 44% ↓
Partners PrEP Study (Kenya, Uganda)	4147 heterosexual HIV discordant couples	Daily oral TDF, TDF-FTC, or placebo	TDF: 67% ↓ TDF-FTC: 75% ↓
TDF2 Study (Botswana)	1219 heterosexual men and women	Daily oral TDF-FTC or placebo	TDF-FTC: 63% ↓
FEM-PrEP (Kenya, South Africa, Tanzania)	2120 women	Daily oral TDF-FTC or placebo	TDF-FTC: no protection
VOICE (South Africa, Uganda, Zimbabwe)	5029 women	Randomized to daily oral TDF, TDF-FTC, oral placebo, TDF vaginal gel, or gel placebo	TDF: no protection TDF-FTC: no protection TDF gel: no protection
Bangkok TDF Study (Thailand)	2413 injection drug users	Randomized to daily oral TDF or placebo	TDF: 49% ↓
IPERGAY (France, Quebec)	400 MSM	Randomized to “on-demand” TDF-FTC or placebo	TDF-FTC: 86% ↓
PROUD (United Kingdom)	545 MSM and transgender women	Randomized to daily oral TDF-FTC immediately or delayed	Immediate TDF-FTC: 86% ↓
iPrEx- Grant RM, et al. <i>N Engl J Med</i> . 2010;363:2587-2599; Partners PrEP - Baeten JM, et al. <i>N Engl J Med</i> . 2012; 367 :399-410; FEM PrEP -Van Damme L, et al. <i>N Engl J Med</i> . 2012 :357 :411-422; TDF 2 - Thigpen MC, et al. <i>N Engl J Med</i> . 2012 ; 367 :423-434 Bangkok TDF study - Choopanya K, et al. <i>Lancet</i> . 2013 ;381 :2083-2090			

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Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



Evidence PrEP Works

PrEP efficacy was measured in:

- 11 randomized control trials (RCT) comparing PrEP with placebo.
- 3 RCTs comparing PrEP with no PrEP (e.g. delayed PrEP or ‘no pill’).
- 3 observational studies.

PrEP was found to be effective in reducing HIV acquisition.

- PrEP was most effective in studies with high adherence.
- Quantifiable drug in plasma increased the efficacy estimates to 74% –92%.

ADHERENCE

PrEP works when taken as prescribed.

Trials where PrEP use was more than 70% demonstrated the highest PrEP effectiveness (risk ratio = 0.30, 95% confidence interval: 0.21–0.45, $P < 0.001$) compared with placebo.³

As the graph above indicates, the higher the percentage of participant samples that had detectable PrEP drug levels, **the greater the efficacy.**

Adherence to drug(s) means that an individual is taking prescribed medications **correctly and consistently**. It involves taking the correct drug:

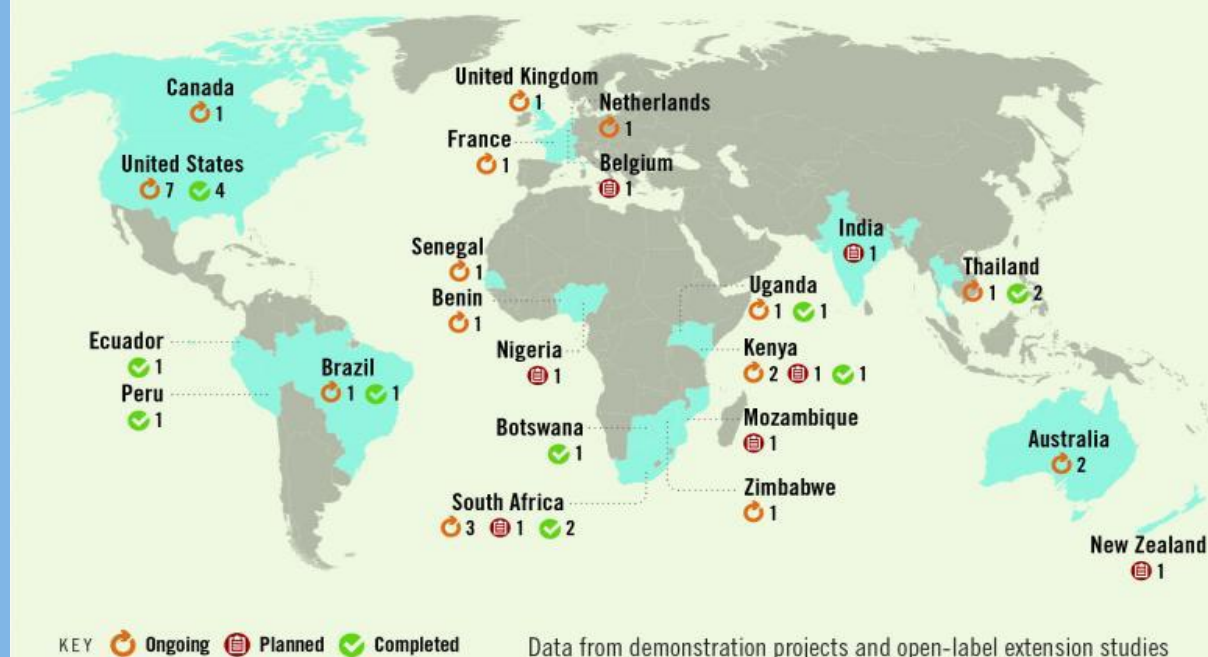
- In the correct dose,
- At a consistent frequency (number of times per day), and
- At a consistent time of day.

Adherence with follow-up means patients attend *all* scheduled clinical visits/procedures, including:

- Clinic and lab assessments.
- Drug collection/repeat prescription.

³ Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV pre-exposure prophylaxis (PrEP) for all populations: A systematic review and meta-analysis. *Aids*. May 5 2016.

Planned, Ongoing and Completed PrEP Evaluation Studies (June 2015)



KEY Ongoing Planned Completed

For the latest on these studies, visit www.avac.org/prep/track-research.

Data from demonstration projects and open-label extension studies are beginning to come in. So far, the findings suggest that people want and will take daily oral PrEP correctly outside of a clinical trial setting. Expanded and faster rollout is key.

<http://www.prepwatch.org/about-prep/research/#ongoingResearch>

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PrEP Regimens

ARVs Recommended for Oral PrEP

- The WHO recommends that oral PrEP regimens should contain tenofovir disoproxil fumarate (TDF).
- According to the WHO, the following regimens should be considered for use as PrEP:

Combined tablet of emtricitabine (FTC) 200 mg / tenofovir disoproxil fumarate (TDF) 300 mg PO Daily

Combined tablet of lamivudine (3TC) 300 mg / tenofovir disoproxil fumarate (TDF) 300 mg PO daily

Single-agent tenofovir disoproxil fumarate (TDF) 300 mg PO daily*
(*Limited evidence on the use of TDF alone for PrEP for MSM)

In <insert country name> the available recommended PrEP regimens include: <insert available regimen>

WHO (2016) Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.

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PrEP Side Effects: Reports from RCTs

In clinical trials, approximately 10% of participants experienced side effects.

The side effects were mild and short-term, and did not persist beyond the first month.

Side effects may include:

- Gastrointestinal (GI) side effects (nausea/vomiting/abdominal pain).
- Creatinine elevation (typically reversible).
- Loss of bone mineral density; recovers after stopping PrEP.

Side Effects Reported from iPrEx Open-label Extension (iPrEx OLE): Observational Study

iPrEx OLE multi-site PrEP cohort taking daily oral TDF/FTC:

- 39% of participants reported any PrEP-related (mainly mild) side effects.
- A “start-up syndrome” has been reported: GI symptoms (nausea, flatulence, diarrhea, abdominal pain, vomiting), headaches, skin problems/itching.

The “start-up syndrome” is transient but can influence adherence:

- Side effects among PrEP users peaked around month one and symptoms are resolved by month three.
- Adherence counseling should focus on the transient nature of a “start-up syndrome”.

RISK BEHAVIORS, HIVDR, AND STIs

Will PrEP encourage people to use condoms less often or to have more sexual partners – i.e. “risk compensation”?

- There was no evidence of this in clinical trials.
- The PROUD study showed that for participants who were at high risk before initiating PrEP, **sexual behavior remained unchanged** whether or not participants received PrEP.

Will PrEP lead to more HIV drug resistance (HIVDR)?

- HIVDR in PrEP users was rare in clinical trials.
 - HIVDR occurred mostly in cases where the person had undiagnosed HIV infection at the time of starting PrEP.
- When adherence to PrEP is high and HIV seroconversion does not occur, HIVDR will not occur.
- If adherence is suboptimal and HIV infection occurs while on PrEP, there can be a risk of HIVDR.
- Optimal adherence to PrEP is crucial.
 - Health providers must support and monitor adherence and teach PrEP users to recognize signs/symptoms of acute HIV infection.

Does PrEP Protect Against Other STI?

- Only condoms protect against STI and pregnancy.
- PrEP protects against HIV and also against herpes simplex virus type 2 in heterosexual populations.
- PrEP does **NOT** protect against syphilis, gonorrhea, chlamydia, or human papilloma virus (HPV).
- PrEP should be provided within a package of prevention services, including STI screening and management, risk reduction counseling, condoms, contraceptives, etc.

MODULE 1 SUMMARY

What we know about PrEP:

- PrEP can be used by HIV uninfected persons to **reduce** the risk of HIV acquisition.
- Daily oral PrEP with TDF-containing regimens is currently recommended.
- PrEP should be taken as an **additional** prevention intervention.
- PrEP is **effective** if taken correctly and consistently.
- PrEP can be used by at risk populations, including heterosexual men and women, MSM, SWs, PWIDs, and transgender women, among others.
- PrEP is **safe** and has minimal side effects.

MODULE 2: PrEP Screening and Eligibility

OBJECTIVES

After completing Module 2, you will be able to:

- Name the 5 main eligibility criteria for PrEP.
- Use the standard medical screening form for PrEP eligibility and substantial risk.
- Name the contraindications for PrEP.
- Explain how to exclude acute HIV infection.

WHO Recommendations

Oral PrEP containing TDF should be offered as an additional prevention choice for people at *substantial risk* of HIV infection as part of combination HIV prevention approaches.¹

¹ WHO (2016) Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.2016

Eligibility for PrEP

Eligibility criteria include:

- HIV seronegative
- No suspicion of acute HIV infection
- At substantial risk* of HIV infection
- Creatinine clearance (eGFR) >60ml/min**
- Willingness to use PrEP as prescribed

* Defined below

** eGFR: estimated glomerular filtration rate. Waiting for creatinine result should not delay initiation of PrEP

HIV SERONEGATIVE

PrEP is a prevention intervention for people who are HIV uninfected.

All persons at substantial risk for HIV and who may be eligible for PrEP should be offered HIV testing prior to PrEP initiation.

HIV testing must be done using national guidelines and algorithms.

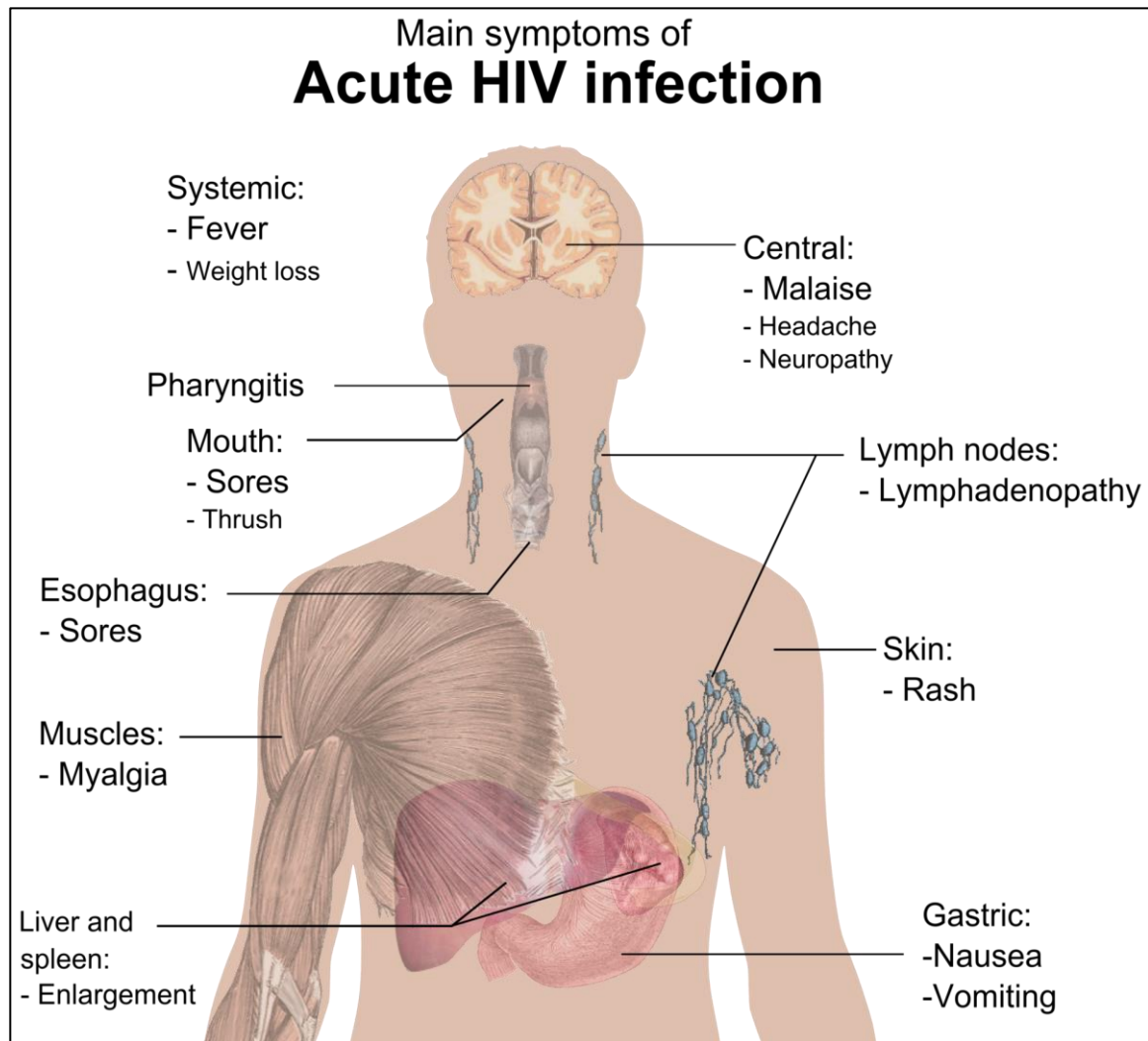
- Ideally, use rapid HIV tests at point of care.
- Promptly link clients who test HIV positive to HIV treatment and care services.

(The trainer will provide the national algorithm.)

NO SUSPICION OF ACUTE HIV INFECTION

Acute HIV infection (AHI) is the **early phase of HIV disease** that is characterized by an initial burst of viremia.

- AHI infection develops **within two to four weeks** after someone is infected with HIV.
- Approximately 40% to 90% of patients with AHI will experience **“flu-like” symptoms**.
 - These symptoms are not specific to HIV, they occur in many other viral infections.
 - Remember that some patients with AHI can be asymptomatic.
- The figure on the next slide depicts some of the presenting signs and symptoms of AHI.
- Do **NOT** start PrEP in clients with suspected AHI.



An estimated 40-90% of patients with acute HIV infection will experience ‘flu-like’ symptoms which usually appear days to weeks after exposure and include:

- Fever
- Fatigue
- Anorexia
- Rash (often erythematous maculopapular)
- Pharyngitis
- Generalized lymphadenopathy
- Mucocutaneous ulceration
- Headache
- Aseptic meningitis
- Radiculitis, myelitis
- May present with OI, thrush, zoster (if CD4 depressed)

These symptoms are not specific to HIV; they occur in many other viral infections. Remember that some patients with acute HIV infection will be asymptomatic.

Diagnosis of AHI

- During AHI, antibodies might be absent or be below the level of detection.
- Serological testing using rapid test might be negative.
- AHI can be diagnosed using “direct” viral tests like HIV RNA or HIV antigen testing.
- In the absence of HIV RNA and antigen testing, PrEP should be deferred for four weeks if AHI is suspected.
- Repeat HIV serological test after four weeks to reassess eligibility.

SUBSTANTIAL RISK FOR HIV INFECTION

Substantial risk for HIV infection (based on history in the past six months)

- Client who is sexually active in a high HIV prevalence population (either in the general population or key population group) **PLUS** reports *ANY* of the following in the past six months:
 - Vaginal or anal intercourse without condoms with more than one partner, OR
 - Sex partner with one or more HIV risk, OR
 - History of an STI (based on lab test, syndromic STI treatment, self-report), OR
 - History of use of post-exposure prophylaxis (PEP)
- OR
- Client who reports history of sharing of injection material/equipment with another person in the past six months.
- OR
- Client who **reports having a sexual partner** in the past six months* who is HIV positive **AND** who has not been on effective HIV treatment.

**On ART for less than six months, or has inconsistent or unknown adherence*

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SCREENING FOR SUBSTANTIAL RISK

- Screening questions should be **framed in terms of people’s behavior** rather than their sexual identity and should **refer to a defined time period (six months, etc.)**.
- It is important for PrEP providers to be **sensitive, inclusive, non-judgmental, and supportive**.
- Be careful not to develop a screening process that might discourage PrEP use.

SAMPLE SCREENING QUESTIONS

General Screening Questions

In the past six months:

- ☐ Have you had sex with more than one sexual partner?
- ☐ Have you had sex without a condom?
- ☐ Have you had sex with people whose HIV status you do not know?
- ☐ Are any of your partners at risk of HIV?
- ☐ Have you had sex with a person who has HIV?

Serodiscordant Couples

For a person who has a partner with HIV:

- ☐ Is your partner taking ART for HIV?
- ☐ Has your partner been on ART for more than six months?
- ☐ Do you discuss your partner's adherence to HIV treatment every month?
- ☐ Do you know your partner's last viral load? What was the result? And when was it done?
- ☐ Do you desire having a child with your partner?
- ☐ Are you and your partner consistently using condoms?

Additional factors

Are there aspects of your situation that may indicate higher risk for HIV? Have you:

- ☐ Received money, housing, food or gifts in exchange for sex?
- ☐ Been forced to have sex against your will?
- ☐ Been physically assaulted, including assault by a sex partner?
- ☐ Taken PEP to prevent HIV infection?
- ☐ Had a sexually transmitted infection (STI)?
- ☐ Injected drugs or hormones using shared equipment?
- ☐ Used recreational/psychoactive drugs?
- ☐ Been required to leave your home?
- ☐ Moved to a new place?
- ☐ Lost your job?
- ☐ Had less than 12 years schooling or left school early?

SERODISCORDANT COUPLES

PrEP can protect the HIV uninfected partner in a heterosexual serodiscordant relationship with an HIV-infected partner if:

- The partner with HIV has been taking ART for less than six months.
 - ART takes three to six months to suppress viral load.
 - In studies of serodiscordant couples, PrEP has provided a useful bridge to full viral suppression during this time.
- The uninfected partner is not confident of the HIV-infected partner's adherence to treatment or has other sexual partners besides the partner on treatment.
- The uninfected partner is aware of gaps in the HIV- infected partner's treatment adherence or the couple is not communicating openly about treatment adherence and viral load test results.

CREATININE AND ESTIMATED CREATININE CLEARANCE

TDF can be associated with a small decrease in estimated creatinine clearance (eGFR) early during PrEP use and usually this does not progress.

PrEP is not indicated if eGFR* is < 60ml/min.

*eGFR: estimated glomerular filtration rate using Cockcroft-Gault equation:

Estimated CrCl = [140-age (years)] x weight (kg) x f where f=1.23 for men and 1.04 for women Serum creatinine (μmol/L)

You can use an online calculator to determine the eGFR:

The screenshot shows a web-based calculator titled "Creatinine Clearance Estimate by Cockcroft-Gault Equation". It features a "Share" link in the top right. The "Input:" section on the left includes: "Sex" with radio buttons for "Male (1)" (selected) and "Female (0.85)"; "Age" with a text input field and a unit dropdown set to "yr"; "Serum Creat" with a text input field and a unit dropdown set to "mg/dL"; and "Weight" with a text input field and a unit dropdown set to "kg". Below these are tabs for "Formula", "Notes", and "References". The "Result:" section on the right displays "Creat Clear" with a unit dropdown set to "mL/min" and "Decimal Precision" set to "2". At the bottom, the formula is shown:
$$\text{CreatClear} = \text{Sex} * ((140 - \text{Age}) / (\text{SerumCreat})) * (\text{Weight} / 72)$$

<http://reference.medscape.com/calculator/creatinine-clearance-cockcroft-gault>

PrEP USE DURING PREGNANCY

- TDF appears to be safe in pregnant women, however, evidence comes from studies of HIV infected women on ART.
- Among HIV uninfected pregnant women, evidence of TDF safety comes from studies of hepatitis B (HBV) mono-infected women.
- PrEP benefits for women at high risk of HIV acquisition appear to outweigh any risks observed to date.
- WHO recommends continuing PrEP during pregnancy and breastfeeding for women at substantial risk of HIV. There is, however, a need for continued surveillance for this population group.

WILLINGNESS TO USE PrEP AS PRESCRIBED

- Education and counseling is provided to support clients to make an informed choice about PrEP.
- Clients should not be coerced into using PrEP.

CLINICAL SCENARIOS

Clinical Scenario 1

Joseph is a 22 year-old man who presents at the clinic because he is interested in starting PrEP. He reports using condoms sometimes during sex with his HIV-positive male partner. His partner is healthy and has been on ART for 4 years. His most recent viral load from “a few months ago” was reported as 1200 copies/mL. Their last unprotected intercourse was last week. Joseph is in good health and is taking no medications. His rapid HIV antibody test today is negative.

- Is Joseph a candidate for PrEP?
- If so, what did you consider in order to determine eligibility?

Clinical Scenario 1

Marie is an 18 year-old woman who presents at the clinic because she feels sick and is afraid she might have HIV. She reluctantly explains that, during the past year, she has been having sex for money or gifts in order to support her two children. Some of her partners have used condoms and others have not. She does not know if her partners have HIV. Marie reports that she has been feeling run down and sick for the past few weeks. Her rapid HIV antibody test today is negative.

- Is Marie a candidate for PrEP?
- If so, why?
- What other information would you need in order to determine eligibility?

Clinical Scenario 3

Geraldine, a 30 year-old wife and mother, presents at the clinic because she has heard that she can get drugs that will prevent her from getting HIV. She suspects that her husband has been injecting drugs, as he has needle marks on his arms. Geraldine is afraid that her husband might have HIV and that he will infect her. She reports that her husband has not been tested. Geraldine’s rapid HIV antibody test today is negative.

- Is Geraldine a candidate for PrEP?
- If so, why?
- What other information might you need in order to determine eligibility?

Clinical Scenario 4

Daniel is a 25 year-old man who presents at the clinic seeking treatment for “blisters.” He reports that, during the past several days, he has had a few painful blisters around his mouth and on his genitals. He declines to report his sexual activity; he says he is a married man and faithful to his wife. He asks if he can take just one pill for the blisters here at the clinic, so that his wife or neighbors do not find out that he is taking pills. Daniel does not want to take any medications ongoing, as his neighbors or church might find out and conclude that he has HIV. He declines to take an HIV test.

- Is Daniel a candidate for PrEP? Why or why not?

SCREENING ROLE-PLAYS

Screening Role-play Scenario 1

Justine is a 19 year-old sex worker with a live-in boyfriend. She was born a male but has been living as a woman since she was 15 years old. She has had sex with multiple partners (men) during the last six months, a few times without condoms. She does not know if she has any STIs, but she has no symptoms.

Justine's boyfriend is living with HIV and he has been on ART for about 1 year. He has adhered to the treatment regimen very well and is in good health. Justine is proud of him for this. Justine and her boyfriend use condoms during sex.

A few weeks ago, Justine was tested for HIV after a scary encounter with a client. The test was negative. Justine has come to the clinic today because she is feeling poorly. She has had a fever and chills in recent days, and wants medicine in order to feel better.

Instructions: Skip sections 1 and 2 of the screening tool. Role-play Sections 3, 4, and 6 of the screening tool. After the role-play, you will complete Section 5 with the whole group. In addition to the question prompts in Section 4, you may need to use other questions such as the ones brainstormed earlier.

Screening Role-play Scenario 2

Lucien is 25 years old. He is a sexually active married man who has sex regularly with his wife, and also with men outside of his marriage. His wife does not know about the sex with men. Lucien insists on using condoms during sex with men, but he does not use condoms with his wife.

Lucien has come to the clinic because the last time he was with a man, the condom broke and he is worried that he might have gotten HIV. He does not know the HIV status of his male sex partners. He assumes that his wife does not have HIV but she has not been tested. He does not use drugs or share injecting material with others.

Instructions: Skip sections 1 and 2 of the screening tool. Role-play Sections 3, 4, and 6 of the screening tool. After the role-play, you will complete Section 5 with the whole group. In addition to the question prompts in Section 4, you may need to use other questions such as the ones brainstormed earlier.

MODULE 2 SUMMARY

PrEP Eligibility, Screening, Side Effects, and Contraindications

- Providers should **inform** and **counsel** potential PrEP users and **conduct an individualized risk assessment**.
- Eligibility for PrEP includes:
 - At substantial risk of HIV infection
 - HIV seronegative
 - No suspicion of acute HIV infection
 - No contraindications to ARVs used in PrEP regimen
 - Willingness to use PrEP as prescribed
- PrEP screening questions should be framed in terms of a person's behavior.
- Side effects in clinical trials were rare and when they occurred they were mild.
- Contraindications for PrEP include:
 - Current or suspected HIV infection
 - Renal impairment as defined by estimated creatinine clearance of <60 ml/min

MODULE 3: Initial and Follow-Up PrEP Visits

OBJECTIVES

By the end of Module 3, you will be able to:

- Specify the procedures for the initial PrEP visit.
- Demonstrate knowledge of national HTS guidelines and local algorithms for HIV testing.
- Describe the rationale and content for brief counseling during the initial PrEP visit.
- Follow the Integrated Next Step Counseling (iNSC) process to counsel clients on sexual health and PrEP adherence.
- Specify the suggested procedures for follow-up PrEP visits.
- Describe the rationale and content for follow-up counseling at each visit.
- Name typical challenges that facilities and providers may face when implementing PrEP, and strategies for addressing them.

INITIAL PrEP VISIT SUGGESTED PROCEDURES

Investigation	Rationale
HIV test (Using algorithm in national HTS guidelines)	<ul style="list-style-type: none"> • Assessment of HIV infection status • Symptom checklist for possible acute HIV infection
Serum creatinine	<ul style="list-style-type: none"> • To identify pre-existing renal impairment
Hepatitis B surface antigen (HBsAg)	<ul style="list-style-type: none"> • To identify undiagnosed hepatitis B (HBV) infection • To identify those eligible for vaccination against hepatitis B
RPR	<ul style="list-style-type: none"> • To diagnose and treat syphilis infection
STI screening	<ul style="list-style-type: none"> • To diagnose and treat STI • Syndromic or diagnostic STI testing, depending on local guidelines
Pregnancy testing	<ul style="list-style-type: none"> • To ascertain pregnancy
Brief counseling	<ul style="list-style-type: none"> • To assess whether the client is at substantial risk for HIV • To assess HIV prevention options and provide condoms and lubricants • To discuss desire for PrEP and willingness to take PrEP • To develop a plan for effective PrEP use, sexual and reproductive health

Initial PrEP Counseling

Initial counseling should focus on:

- **Increasing awareness** of PrEP as a choice
- **Helping the client to decide** whether PrEP is right for them
- **Preparing individuals** for starting PrEP
- **Explaining** how PrEP works
- **Providing basic recommendations**
- The importance of **adherence** and **follow-up visits**
- **Potential PrEP side effects**
- Recognizing symptoms of **acute HIV infection**
- Building a **specific plan** for PrEP
- Discussing **sexual health and harm reduction measures**
- Explaining the need for **repeat clinic visits** and **repeat blood tests**

Additional information for women:

- PrEP does not affect the efficacy of hormonal contraceptives.
- PrEP does not protect against pregnancy.
- PrEP can be continued during pregnancy and breastfeeding.

PrEP Counseling

During the counseling session “Assess client understanding that **the protection provided by PrEP is not complete, and does not prevent other STIs or unwanted pregnancies, and therefore PrEP should be used as part of a package of HIV prevention services** (inclusive of condoms, lubrication, contraception, risk reduction counseling and STI management).¹”

Source: From the Southern African Clinician Society Guidelines for Provision of PrEP

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Key Initial Visit Counselling Messaging: PrEP Efficacy

PrEP works when taken!

PrEP reaches maximum effectiveness after seven daily doses.

PrEP does not prevent most sexually transmitted infections other than HIV. Condoms used with every act of sexual intercourse provides some protection against many of these infections.

PrEP does not prevent pregnancy. Use effective contraception unless you want pregnancy.

PrEP is safe.

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Key Initial Visit Counselling Messaging: Supporting Adherence

Taking PrEP each day is easiest if you make taking the tablets a daily habit, linked to something else that you do every day without fail.

If you forget to take a tablet, take it as soon as you remember.

PrEP tablets can be taken any time of day, with food or without food.

PrEP is safe and effective even if you are taking hormonal contraceptives, sex hormones or non-prescription drugs.

- Drinking alcohol will not affect the safety or effectiveness of PrEP. But drinking alcohol could make you forget to take the PrEP tablets.

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SUPPORTING ADHERENCE

Common Reasons for Low Adherence to ART

Individual Factors	Medication Factors	Structural Factors
<ul style="list-style-type: none"> • Forgetting doses • Being away from home • Changes in daily routines • Depression or other illness • Limited understanding of treatment benefits • Lack of interest or desire to take the medicines • Substance or alcohol use • Absence of supportive environment • Fear of stigma and discrimination 	<ul style="list-style-type: none"> • Adverse events • Complexity of dosing regimens • Pill burden • Dietary restrictions (PrEP will require taking just one tablet daily and there are no dietary restrictions) 	<ul style="list-style-type: none"> • Distance to health services • Access to pharmacies • Long waiting times to receive care and obtain refills • Burden of direct and indirect costs of care

Voluntary vs. Involuntary Non-adherence

Voluntary Non-Adherence	Involuntary Non-Adherence
<ul style="list-style-type: none"> • Not convinced PrEP is needed • Does not believe PrEP works or is working • Does not like taking pills • Has experienced side-effects; wishes to avoid side effects • Has experienced stigma while taking PrEP • Does not believe it is necessary to take every day • Does not want to take with alcohol or other drugs • Wishes to avoid others witnessing pill-taking 	<ul style="list-style-type: none"> • Forgot to take pill • Forgot to refill prescription • Has competing priorities (e.g. employment, child care) • Has difficulty with personal organization and scheduling • Affected by depression or other unaddressed mental illness • Can not afford PrEP (in settings where clients pay for PrEP services) • Does not want/has no time/cannot afford to come to health care facility • Dissatisfaction with health care provider interactions • No place to store medication • Unaddressed substance use issues, especially dependence on alcohol or other drugs • Insufficient food to take pills

Adherence Lessons from ART Programs

Health providers can **positively influence adherence** by:

- Facilitating accurate knowledge and understanding of medication benefits and requirements
- Preparing for and managing side-effects
- Monitoring of adherence
- Identifying social support
- Encouraging medication optimism
- Building self-efficacy for adherence
- Developing a routinized daily schedule in which to integrate regular dosing
- Maintaining an open line of communication with PrEP clients

Approaches to PrEP Medication Adherence Support

Support Issue:	Provider Options:
Adequate and accurate PrEP knowledge	<ul style="list-style-type: none"> Briefly explain or provide materials about: <ul style="list-style-type: none"> Indications for medication. The anticipated risks and benefits of taking medication. How to take it (one pill per day). What to do if one or more doses are missed. Assess for misinformation.
Preparing for and managing side effects	<ul style="list-style-type: none"> Educate about what side effects to expect, for how long, and how to manage them. Educate about the signs and symptoms of acute HIV infection and how to obtain prompt evaluation and care.
Fostering self-efficacy	<ul style="list-style-type: none"> Foster discussion of personal perception of HIV risks. Recommend or provide medication-adherence tools: <ul style="list-style-type: none"> Pill boxes Phone apps, pager, or SMS reminder services
Routinized daily schedule	<ul style="list-style-type: none"> Discuss how to integrate daily dose with other daily events and what to do when away from home.
Provider support	<ul style="list-style-type: none"> Regularly assess adherence. Ask for a patient self-report. Complete the prescription/visit record. Use new technologies (text reminders). Offer allied clinical support services (e.g., pharmacist).
Social Support	<ul style="list-style-type: none"> Discuss privacy issues for the PrEP user. Offer to meet with partners or family members if they are supportive.
Mental health and substance abuse	<ul style="list-style-type: none"> Consider screening for depression or substance-abuse problems. Provide or refer to indicated mental health or substance-abuse treatment and relapse-prevention services.
Population-specific challenges	<ul style="list-style-type: none"> Consider additional medication-adherence support for: <ul style="list-style-type: none"> Adolescents. People with unstable housing. Transgender women. Others with specific stressors that may interfere with medication adherence.

Adherence Assessment and Promotion

Ask about adherence at each visit:

- Encourage the PrEP user to self-report in order to understand what they believe about their adherence.
- Ask about adherence over the last three days (short recall).
- Avoid judgment to encourage a realistic and honest description.

Additional methods to monitor adherence:

- Pharmacy refill history
- Pill-count
- Blood level of drugs
- Hair sample to test drug-level

Several approaches can be used to promote adherence:

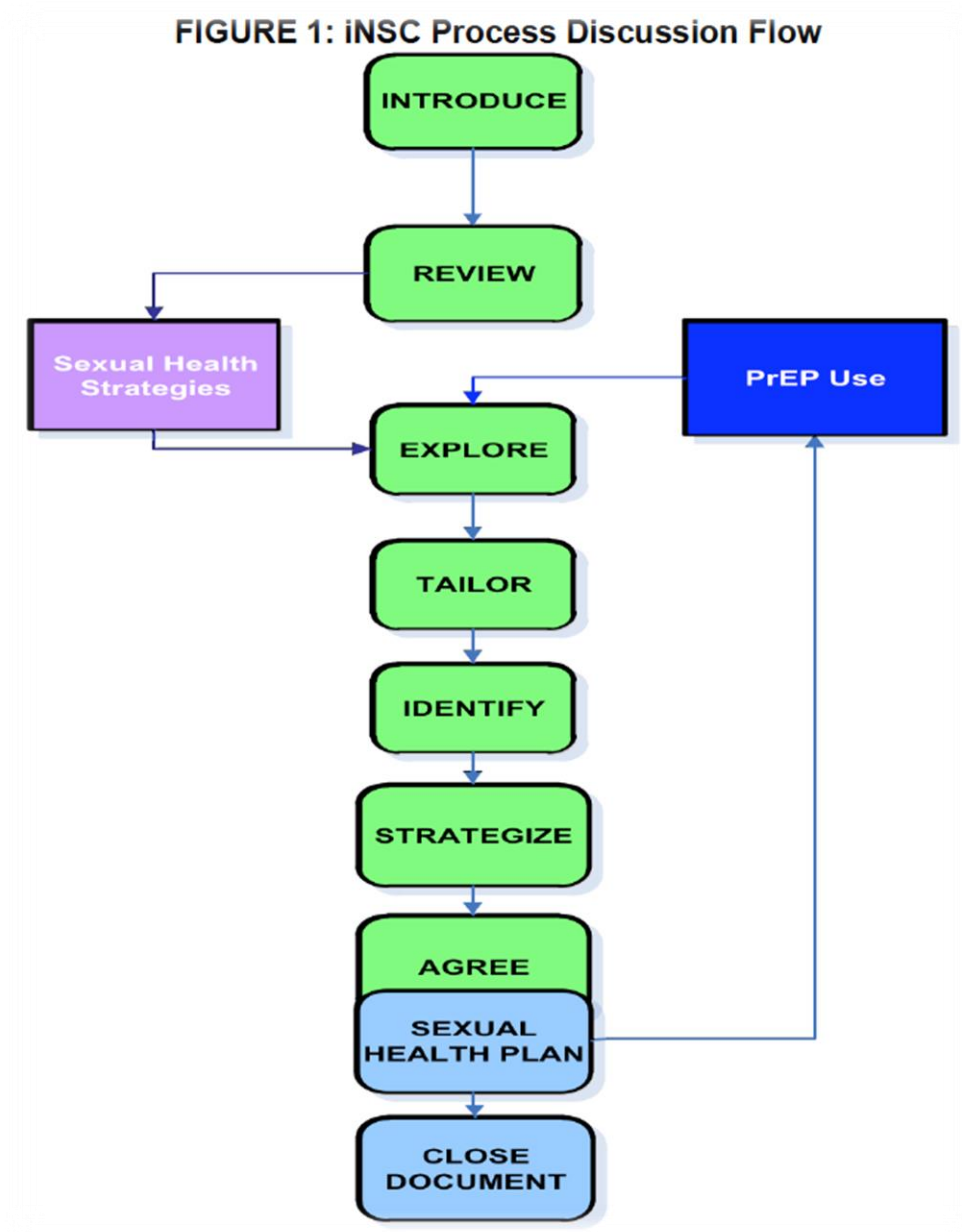
- Motivational interviewing
- Informed Choice Counseling (ICC)
- **Integrated Next Step Counseling (iNSC)**

INTEGRATED NEXT STEP COUNSELING (iNSC)

Integrated next step counseling (iNSC) was used in the iPrEx OLE study to counsel individuals on sexual health promotion more generally, **with specific emphasis on PrEP adherence for individuals on PrEP.**

Implementation of iNSC is positioned with delivery of negative HIV test results and serves as pre/post-test HIV counseling as well as adherence counseling in **one brief, targeted, tailored conversation.**

This is the recommended flow for a step-by-step counseling process that leads to clear strategies and formal plans for PrEP use and non-PrEP-related sexual health:



iNSC Steps, Components, and Examples

iNSC Step	Critical Components	Example Prompts
Introduce the counseling session	<ul style="list-style-type: none"> • Explain what you're talking about and why • Get permission to proceed 	<i>I would like to take a few minutes to check in with you about your goals and how to meet them. Is that okay?</i>
Review client's experiences	<ul style="list-style-type: none"> • Ask about what the client already knows about PrEP and how they learned it 	<i>Thank you. Can you tell me a little about what you have heard about PrEP and about your experiences with PrEP?</i>
Explore context of client-specific facilitators and barriers	<ul style="list-style-type: none"> • Use open-ended questions to explore factors or situations that help make pill-taking a little easier; and those that make it harder or a little more difficult 	<i>What seems to make PrEP easy to take or harder to take?</i>
Tailor the discussion to focus on increasing ease of pill-taking	<ul style="list-style-type: none"> • This is a pause to allow the provider/counselor to consider what information gathered in earlier steps is used to tailor the next question 	<i>Let me think for a moment about what you have said.</i>
Identify adherence-related needs	<ul style="list-style-type: none"> • Guide the conversation towards identifying participant perceptions of what would help to best integrate PrEP use into their daily life 	<i>Given everything going on right now, what would need to happen for it to feel a little easier to work this regimen into your daily life?</i>
Strategize with the participant on the next step	<ul style="list-style-type: none"> • Work with participant so that they identify one or a few viable strategies for increasing effective PrEP use 	<ul style="list-style-type: none"> • <i>How could that happen?</i> • <i>What are some ideas for how you could approach that?</i>
Agree on which strategy will be tried next	<ul style="list-style-type: none"> • Ask participant which strategy(ies) they are willing to try or continue using 	<i>Of the things that we have talked about, which might you be willing to try between now and the next time we meet?</i>
Close/document	<ul style="list-style-type: none"> • Provide a summary of the discussion and thank the patient 	<i>What I'm hearing is that _____ would really make it feel easier to work PrEP into your life and that you'll give it a try between now and the next time we meet. Thank you for talking with me and I look forward to talking again.</i>

Amico K R, McMahan V, Goicochea P, et al. Supporting study product use and accuracy in self-report in the iPrEx study: next step counseling and neutral assessment. *AIDS and behavior*. Jul 2012;16(5):1243-1259.

iNSC ROLE PLAYS

iNSC Role-play Scenario 1

Geraldine, a 30 year-old wife and mother, is interested in starting PrEP. She presented at the clinic because she heard that she could get drugs that will prevent her from getting HIV. She suspects that her husband has been injecting drugs and has needle marks on his arms. Geraldine is afraid that her husband might have HIV and that he will infect her. She reports that her husband has not been tested. Geraldine's rapid HIV antibody test today was negative. She is eager to start PrEP but is worried that her husband might see her taking pills and become abusive or make her stop taking the medication.

iNSC Role-play Scenario 2

Joseph is a 22 year-old man who presented at the clinic because he is interested in starting PrEP. He reports using condoms sometimes during sex with his HIV-positive male partner. His partner is healthy and has been on ART for 4 years. His most recent viral load from "a few months ago" was reported as 1200 copies/mL. Their last unprotected intercourse was last week. Joseph is in good health and is taking no medications. His rapid HIV antibody test today was negative. Joseph reports that he loves to live life from moment to moment. He says that he is not good at "following orders" and is worried that he might forget to take his pills.

Key Initial Visit Consideration: Drug Supply

- Providing an **extra month's supply of medication at the first visit** will assure an adequate supply for daily dosing until the next visit.
- This is important in case the follow-up visit is delayed for any reason.

Patients who have some medication supply in reserve
tend to show better adherence!

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PREP FOLLOW-UP VISITS

- Clients on PrEP require regular visits with the health provider.
- Programs should decide on the optimal frequency of visits for monitoring PrEP use.
- It is suggested to have a follow-up visit:
 - One month after initiating PrEP, and
 - Thereafter every three months.
- Outside regular monitoring visits, clients should also consult if they have severe adverse events or signs/symptoms of AHI.

PrEP Follow-up Visit Procedures

Intervention	Schedule following PrEP initiation
Confirmation of HIV-negative status	<ul style="list-style-type: none">• Every three months (consider also testing at one month if HIV RNA or antigen testing was not performed before starting PrEP)
Address side-effects	<ul style="list-style-type: none">• Every visit
Brief adherence counseling	<ul style="list-style-type: none">• Every visit
Estimated creatinine clearance	<ul style="list-style-type: none">• At least every six months, or more frequently if there is a history of conditions affecting the kidney, such as diabetes or hypertension
	<ul style="list-style-type: none">• Provide STI screening, condoms, contraception as needed.• Counsel regarding symptoms of acute HIV infection, and to come back as soon as possible for evaluation if these symptoms occur.

Repeat HIV Testing

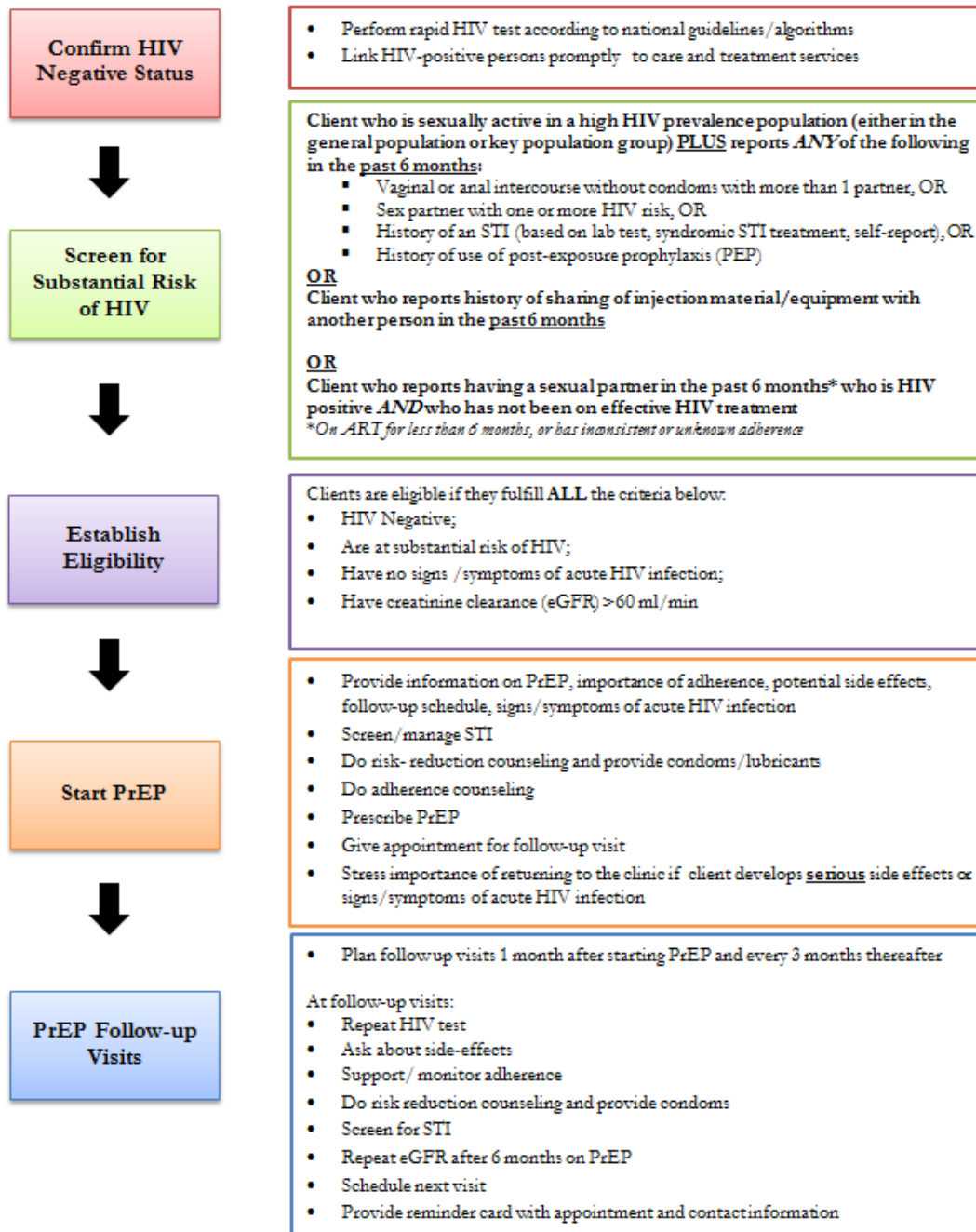
- Repeat HIV testing is needed to inform decisions on whether to continue or discontinue PrEP.
- Repeat HIV testing (using national guidelines):
 - One month after starting PrEP
 - Every three months thereafter
- Remember the limitation of serological tests during AHI in the window period (time from HIV infection to detection of antibodies), and also that exposure to ARVs can decrease sensitivity of serological tests.
- Stop PrEP if AHI is suspected.

Follow-up PrEP Counseling

Follow-up counseling should focus on:

- Checking in on the **current context** of sexual health
- The patient's **desire to remain on and assessment of continued risk of PrEP**
- **Facilitators** and **barriers** to PrEP use
- Additional **non-PrEP related sexual health protection** strategies (condoms, etc.)
- **Dosing requirements** for highest protection
- What to do **if a dose is missed**
- Common **adherence strategies**
- Reasons for **ongoing monitoring** while on PrEP
- How to recognize symptoms of **acute HIV infection**
- **Side-effects & side-effects management**
- How to **safely discontinue** and **restart** PrEP as appropriate

PrEP Clinical Pathway



MODULE 3 SUMMARY

- Prescribe PrEP as part of a comprehensive HIV prevention strategy.
- Confirm a negative HIV test immediately prior to initiating PrEP.
- Ensure there are no contra-indications to PrEP.
- Ensure clients have correct information about PrEP.
- Develop an adherence support plan with the client and monitor adherence at each visit.
- Conduct risk-reduction counseling at each visit.

MODULE 4: Monitoring and Managing PrEP Side Effects, Seroconversion, and Stigma

OBJECTIVES

After completing Module 4, you will be able to:

- Explain how to manage creatinine elevation.
- List additional causes of creatinine elevation.
- Explain how to manage seroconversion.
- Develop strategies to minimize PrEP stigma.
- Give examples of gaps in knowledge about PrEP.
- Describe how M&E tools might be adapted for local use.

MONITORING AND MANAGING CREATININE ELEVATION

Approximately 1 in every 200 PrEP users may develop an elevation of serum creatinine. This is defined as a 50% increase above baseline or an elevation above the normal range. Renal impairment is defined as having an estimated creatinine clearance of <60 ml/min.

Creatinine elevations have usually **reversed** after stopping PrEP. It is important to monitor **transient creatinine elevation** and for signs of **chronic or severe renal insufficiency**.

To manage creatinine elevation:

- Discontinue PrEP if creatinine elevation is confirmed on a separate specimen and if estimated creatinine clearance decreases to <60 ml/min.
- After PrEP is stopped, creatinine should be checked for another one to three months and PrEP restarted if eGFR returns to > 60 ml/min.
- Additional causes and management of creatinine elevations should be considered if:
 - Creatinine elevations are more than 3x the baseline.
 - Renal function or creatinine elevations do not return to normal levels within three months after stopping PrEP.
 - Creatinine elevations progress at one month or more after stopping PrEP.
- Common causes of chronic or severe renal insufficiency include: diabetes mellitus, uncontrolled systemic hypertension, hepatitis C infection, liver failure, and preeclampsia during pregnancy.

SEROCONVERSION ON PrEP

- PrEP works when taken. In clinical trials, the level of protection was strongly correlated with adherence.
- HIV infection can be prevented with consistent use of PrEP.
- HIV seroconversion after prescribing PrEP can occur if PrEP is not used correctly or consistently, or if HIV infection was undiagnosed at the time of PrEP initiation.
- Part of counseling should include information to help PrEP users recognize signs/symptoms of AHI, which should prompt a clinic visit without delay.

Managing Seroconversion

- If a person using PrEP tests positive for HIV, PrEP should be **stopped immediately** and the person referred for prompt initiation of HIV treatment.
- Transitions from PrEP to HIV treatment without a gap avoid the risk of resurgence in viral load, immunological injury, and secondary transmissions.

PrEP SPECIAL SITUATIONS

Situation	Recommendation/Follow-Up
Hormonal Contraception	<ul style="list-style-type: none">• PrEP does not affect the efficacy of hormonal contraceptives and hormonal contraceptives do not affect PrEP efficacy.
Pregnancy and breastfeeding	<ul style="list-style-type: none">• PrEP may be continued during breastfeeding in women who are at substantial risk for HIV acquisition.
Hepatitis B infection	<ul style="list-style-type: none">• Hepatitis B vaccination is appropriate for people at substantial risk for HBV or HIV infection.
Management of Recent HIV Exposure with PEP	<ul style="list-style-type: none">• People who have been exposed to HIV in the past 72 hours should be offered post-exposure prophylaxis (PEP).• WHO recommends PEP consisting of TDF/3TC (or FTC), preferably combined with a boosted protease inhibitor, for 28 days (use national guidelines).• PEP should be transitioned to PrEP after 28 days if the HIV test remains negative and there is substantial ongoing risk of HIV acquisition.

Minimizing PrEP Stigma

- Confidentiality is essential in PrEP services.
- People may face stigma if their PrEP use becomes known.
- PrEP use can exacerbate stigma if others mistakenly consider PrEP use to be evidence of irresponsible behavior or mistakenly think that PrEP is HIV treatment.
 - Such stigma will decrease PrEP uptake and adherence among people who would otherwise benefit from it.

Presenting PrEP to your communities as a *responsible choice* that *protects both partners* will increase the impact of PrEP, prevent more HIV infections, and can help reduce stigma.

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CURRENT GAPS IN PrEP KNOWLEDGE AND NEED FOR CONTINUED SURVEILLANCE

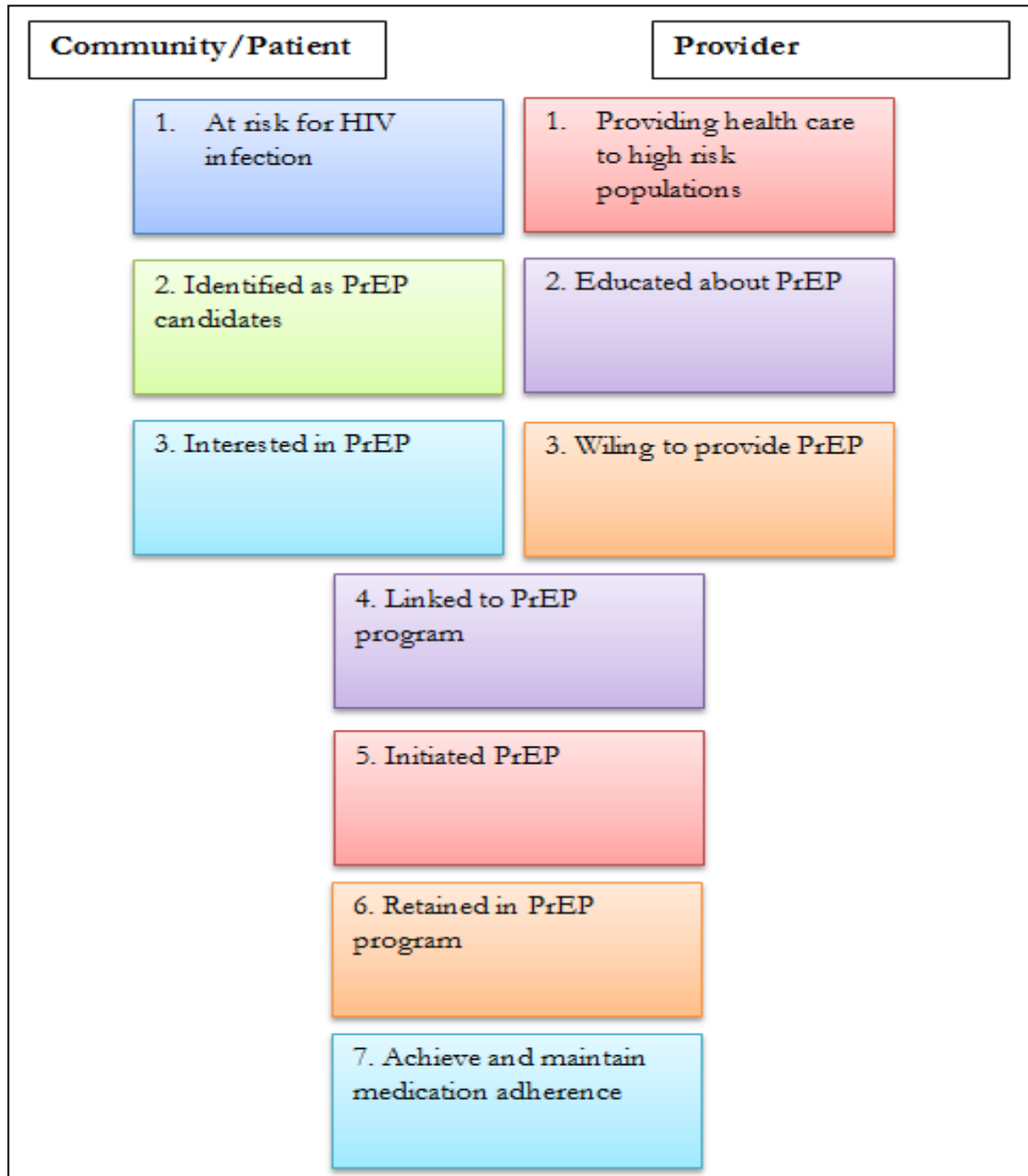
Current gaps in knowledge related to implementation of PrEP include:

- **Renal safety** of FTC/TDF PrEP in people with diabetes mellitus and uncontrolled systemic hypertension has not been evaluated.
- Although 3TC is equivalent to FTC for HIV treatment, **use of 3TC in combination with TDF for PrEP** has not been studied.
- **Comparison of daily vs. on-demand PrEP regimens** is still limited.
- Effectiveness of **on-demand oral PrEP regimens for women** has not been evaluated.
- Although cases of **clinical HBV rebound** when stopping FTC/TDF PrEP have not been observed among people with current HBV infection in clinical trials, most trials excluded such individuals.

Need for Continued Surveillance

The benefits of PrEP in women at substantial risk of HIV acquisition appear to outweigh any risks observed to date, however, there is a need for continued surveillance of maternal, pregnancy and infant outcomes to confirm the safety that studies to date suggest.

PrEP CASCADE



MODULE 4 SUMMARY

- PrEP users should be informed about how to recognize signs and symptoms of acute HIV infection.
- If persons using PrEP test positive for HIV, stop PrEP immediately and start ART as soon as possible, without a gap after PrEP is discontinued.
- If confirmation of positive HIV test result is delayed for more than a few hours, transition to fully suppressive ART (three ARVs as per national treatment guidelines).
- Ideally, blood creatinine (eGFR) should be measured before starting PrEP and **at least every six months** after PrEP is started. Initiation of PrEP should not be delayed while waiting for creatinine result.

MODULE 5: Post-Test, Evaluation, and Closing

The trainer will provide the post-test and Training Evaluation Form.

MODULE 6: PrEP Monitoring & Evaluation Tools

OBJECTIVES

After completing Module 6, you will be able to:

- Complete the PrEP Facility Record, PrEP Follow-up Visits Form, and the PrEP Client register correctly.
- Complete the PrEP Monthly Summary Form and PrEP Quarterly Cohort Report correctly.
- Describe how PrEP M&E tools might be adapted for local use.

MONITORING AND EVALUATION (M&E) FORMS

The forms covered in this module are:

- PrEP Facility Record
- PrEP Follow-up Visits Form
- PrEP Client Register
- PrEP Monthly Summary Form
- PrEP Quarterly Cohort Report

M&E PRACTICE SCENARIOS

M&E Scenario 1

Joseph is a 22 year-old man who presented at the clinic because he is interested in starting PrEP. He reports using condoms sometimes during sex with his HIV-positive male partner. His partner is healthy and has been on ART for 4 years. His most recent viral load from “a few months ago” was reported as 1200 copies/mL. Their last unprotected intercourse was last week. Joseph is in good health and is taking no medications. His rapid HIV antibody test today was negative. Joseph reports that he loves to live life from moment to moment. He says that he is not good at “following orders” and is worried that he might forget to take his pills. Joseph has agreed to start PrEP.

M&E Scenario 2

Marie is an 18 year-old woman who presented at the clinic because she feels sick and is afraid she might have HIV. She reluctantly explains that, during the past year, she has been having sex for money or gifts in order to support her two children. Some of her partners have used condoms and others have not. She does not know if her partners have HIV. Marie reports that she has been feeling run down and sick for the past few weeks. Her rapid HIV antibody test today is negative. After you determine that there is no suspicion of AHI, Marie has agreed to start PrEP.

M&E Scenario 3

Geraldine, a 30 year-old wife and mother, is interested in starting PrEP. She presented at the clinic because she heard that she could get drugs that will prevent her from getting HIV. She suspects that her husband has been injecting drugs, as he comes home with needle marks on his arms. Geraldine is afraid that her husband might have HIV and that he will infect her. She reports that her husband has not been tested. Geraldine’s rapid HIV antibody test today was negative. She is eager to start PrEP but is worried that her husband might see her taking pills and become abusive or make her stop taking the medication. Geraldine has agreed to start PrEP.

M&E Scenario 4

Gabrielle is a 25 year-old married woman. She has come to the clinic distressed because of her husband’s behaviour. Lately, he has been staying out all night sometimes. When he returns he has needle marks on his arms. She is afraid that he might be using drugs. Gabrielle has come to the clinic to get medicine to protect against any infection that her husband might have. She feels that she cannot control his behaviour, but she can try to protect herself.

Despite the problems with her husband, Gabrielle has sex (vaginal) with her husband almost every week. Her husband does not like to use condoms. Gabrielle does not know if her husband has HIV or not, as he refuses to get tested; he says that such tests are for “bad people.” She fears, though, that he may be having sex with other women.

Gabrielle has not had any STIs. She has not taken PEP. She does not use drugs or share injecting material with others. She last had sex with her husband 2 nights ago. She feels fine and does not have a fever, or cold or flu-like symptoms. Her rapid HIV antibody test today is negative. Gabrielle has decided to start PrEP.

M&E Scenario 5

Justine is a 19 year-old sex worker with a live-in boyfriend. She was born a male but has been living as a woman since she was 15 years old. She has had sex with multiple partners (men) during the last six months, a few times without condoms. She does not know if she has any STIs, but she has no symptoms.

Justine's boyfriend is living with HIV and he has been on ART for about 1 year. He has adhered to the treatment regimen very well and is in good health. Justine is proud of him for this. Justine and her boyfriend use condoms during sex.

A few weeks ago, Justine was tested for HIV after a scary encounter with a client. The test was negative. Justine has come to the clinic today because she is feeling poorly. She has had a fever and chills in recent days, and wants medicine in order to feel better. You determine that there is no suspicion of AHI. Justine agrees to start PrEP.

M&E Scenario 7

Lucien is 25 years old. He is a sexually active married man who has sex regularly with his wife, and also with men outside of his marriage. His wife does not know about the sex with men. Lucien insists on using condoms during sex with men, but he does not use condoms with his wife.

Lucien has come to the clinic because the last time he was with a man, the condom broke and he is worried that he might have gotten HIV. He does not know the HIV status of his male sex partners. He assumes that his wife does not have HIV but she has not been tested. He does not use drugs or share injecting material with others. Lucien's HIV test is negative. He agrees to start PrEP.

M&E Scenario 7

Anne is a sex worker and is interested in starting PrEP. She uses condoms during sex with commercial clients but not with her stable partner of unknown HIV status. She had a negative HIV test 6 months ago and wants to avoid HIV infection, as she would like to have a baby with her partner. She is using injectable hormonal contraceptive as she used to forget to take oral contraceptives on a daily basis. Anne's HIV test is negative. She has decided to start PrEP.

SAMPLE DATA FOR PrEP MONTHLY SUMMARY FORM

Clients who received HIV testing for PrEP screening

Gender	Age	HIV status	Situation
Female	21	Negative	Male partner is HIV positive
Female	18	Positive	Sex worker
Male	35	Negative	Injects drugs; AHI suspected
Female	17	Negative	Was born a male
Male	19	Negative	Has sex with men
Male	25	Negative	Female partner is HIV positive
Female	31	Negative	Husband has sex with men
Female	26	Negative	Was born a male
Male	45	Positive	has sex with men
Female	20	Negative	Sex worker
Male	28	Negative	Has sex with SW; AHI suspected
Male	23	Negative	Has sex with men
Female	32	positive	Injects drugs
Male	22	Negative	Sex worker
Female	52	Negative	Husband has sex with sex workers
Female	19	Negative	Injects drugs

Clients who started PrEP

- Determine based on HIV test results and AHI information above.

Returning PrEP clients who received follow-up HIV testing

Gender	Age	HIV status	Situation	Follow-up test
Female	21	Negative	Male partner is HIV positive	Negative
Female	18	Positive	Sex worker	
Male	35	Negative	Injects drugs; AHI suspected	Negative
Female	17	Negative	Was born a male	Negative
Male	19	Negative	Has sex with men	Negative
Male	25	Negative	Female partner is HIV positive	Negative
Female	31	Negative	Husband has sex with men	Positive
Female	26	Negative	Was born a male	Negative
Male	45	Positive	has sex with men	Positive
Female	20	Negative	Sex worker	Negative
Male	28	Negative	Has sex with SW; AHI suspected	Positive
Male	23	Negative	Has sex with men	Negative
Female	32	Positive	Injects drugs	
Male	22	Negative	Sex worker	Positive
Female	52	Negative	Husband has sex with sex workers	Negative
Female	19	Negative	Injects drugs	Negative

INSTRUCTIONS FOR PrEP QUARTERLY COHORT REPORT

- Use your completed PrEP Monthly Summary Form and the information below to complete the PrEP Quarterly Cohort Report for Cohort 1.
 - Transferred in: Female, age 24, HIV status negative, sex worker.
 - Transferred in: Male, age 55, HIV status negative, has sex with men.
 - Female, age 19, injects drugs, stopped PrEP due to positive HIV test.
 - No PrEP clients stopped because they were no longer at substantial risk.
 - Male, 45, has sex with men, was lost.
 - No PrEP clients from this cohort died.

Appendices:

A. Pre-Test Assessment

B. Post-Test Assessment

C. Materials in Participant Folders

D. PrEP Clinical Pathway

E. Screening for Substantial Risk of HIV infection

F. Provider Checklist for Initial PrEP Visit

G. Provider Checklist for Follow-up PrEP Visit

B. Post- Test Assessment for PrEP Training for Providers in Clinical Settings

Please tick the correct answers to each multiple choice question below:

1. Pre-Exposure Prophylaxis (PrEP) is the use of antiretroviral drugs (ARVs):

(select all that apply, if applicable)

- a) To prevent mother-to-child transmission of HIV
- b) To prevent HIV infection after potential exposure to HIV
- c) By HIV-negative persons to prevent HIV acquisition
- d) To treat HIV infection in men who have sex with men

2. Which of the following statements is true?

(select all that apply, if applicable)

- a) Antiretroviral therapy (ART) has not been shown to have prevention benefits
- b) Pre-Exposure Prophylaxis (PrEP) and antiretroviral therapy (ART) are both used by HIV infected persons
- c) Post-exposure prophylaxis (PEP) and Pre-Exposure Prophylaxis (PrEP) are both used by HIV negative persons to prevent HIV acquisition
- d) Pre-Exposure Prophylaxis (PrEP) should be used by health care workers after needle stick injuries to prevent HIV infection

3. Pre-Exposure Prophylaxis (PrEP) should be used:

(select all that apply, if applicable)

- a) As part of a comprehensive HIV-1 prevention strategy that includes other preventive measures
- b) In individuals who have a confirmed negative HIV test
- c) Only by key populations
- d) Only by non-pregnant women

4. The following antiretroviral drugs can be used for Pre-Exposure Prophylaxis (PrEP):

(select all that apply, if applicable)

- a) Tenofovir/emtricitabine (TDF/FTC)
- b) Tenofovir/emtricitabine + Efavirenz (TDF/FTC) +(EFV)
- c) Tenofovir/lamivudine (TDF/3TC)
- d) Zidovudine/lamivudine (AZT/3TC)

5. Pre-Exposure Prophylaxis (PrEP) should be discontinued if:

(select all that apply, if applicable)

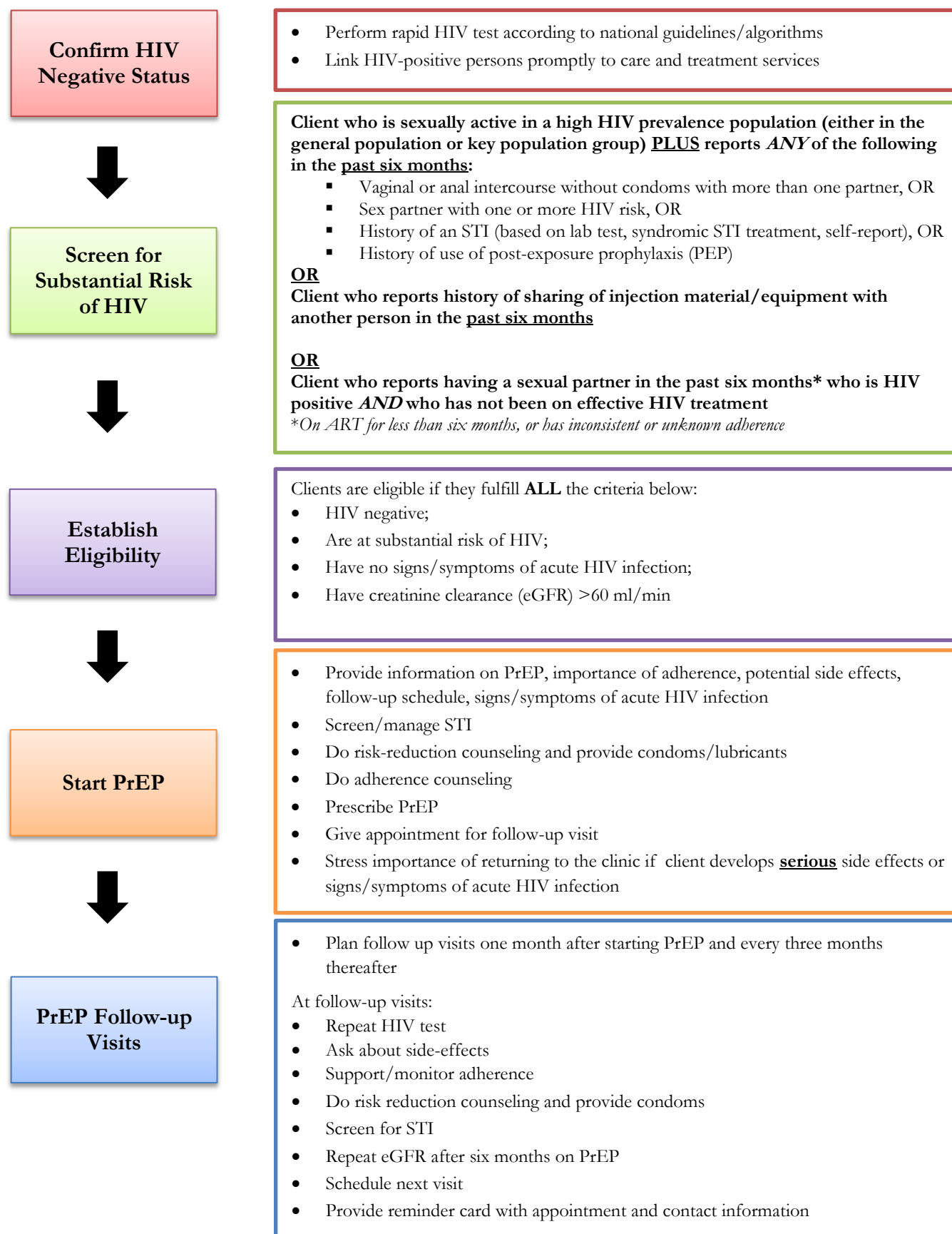
- a) The client falls pregnant
- b) The estimated glomerular filtration rate (eGFR) decreases to <60 ml/min
- c) The client reports headaches and stomach upset
- d) The client tests HIV positive

C. Materials in Participant Folders

Each participant folder should include the following:

1. Pre-Test Assessment
2. Post-Test Assessment
3. Training Evaluation Form
4. PrEP Clinical Pathway
5. Screening for Substantial Risk of HIV Infection Chart
6. Provider Checklist for Initial PrEP Visits
7. Provider Checklist for Follow-up PrEP Visits
8. PrEP M&E Tool Package, which includes:
 - a. PrEP Screening for Substantial Risk and Eligibility
 - b. PrEP Facility Record
 - c. PrEP Patient Register
 - d. PrEP Monthly Summary Form
 - e. PrEP Quarterly Cohort Report

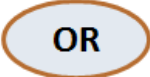
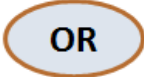
D. PrEP Clinical Pathway



E. Screening for Substantial Risk of HIV Infection

SCREENING FOR SUBSTANTIAL RISK of HIV INFECTION

(Based on history in the past six months)

- **Client who is sexually active in a high HIV prevalence population (either in the general population or key population group) PLUS reports *ANY* of the following in the past 6 months:**
 - Vaginal or anal intercourse without condoms with more than 1 partner, OR
 - Sex partner with one or more HIV risk, OR
 - History of an STI (based on lab test, syndromic STI treatment, self-report), OR
 - History of use of post-exposure prophylaxis (PEP)
- 
- **Client who reports history of sharing of injection material/equipment with another person in the past 6 months**
- 
- **Client who reports having a sexual partner in the past 6 months* who is HIV positive *AND* who has not been on effective HIV treatment**
 - *On ART for less than 6 months, or has inconsistent or unknown adherence*

F. Provider Checklist for Initial PrEP Visit

Provider Checklist for Initial PrEP Visit

- ☐ **HIV test (using algorithm in national HIV Testing guidelines)**
 - Assessment of HIV infection status
- ☐ **Exclude acute HIV infection**
 - Ask about last potential exposure to HIV
 - Ask/look for 'flu-like' symptoms
- ☐ **Screen for substantial HIV risk**
- ☐ **Serum creatinine (calculate eGFR)**
 - To identify pre-existing renal impairment
- ☐ **Hepatitis B surface antigen (HBsAg) – if available**
 - To identify undiagnosed Hepatitis B (HBV) infection
 - To identify those eligible for vaccination against Hepatitis B
- ☐ **STI screening**
 - Perform syndromic or etiological STI testing (depending on local guidelines)
 - Rapid Plasma Reagin test (RPR) for syphilis (if available)
- ☐ **Pregnancy test**
 - Ask about last menstrual period (perform pregnancy test if needed)
- ☐ **Conduct risk reduction counseling**
 - Clients will be referred based on specific needs, i.e. social support, harm reduction, gender-based violence programs, etc.
- ☐ **Provide information on PrEP and conduct adherence counseling**
- ☐ **Provide condoms and lubricants**
- ☐ **Provide (or refer to) reproductive health services (as needed)**
- ☐ **Schedule next appointment (provide appointment card)**

Please adapt this checklist to align with national guidelines on PrEP

G. Provider Checklist for Follow-up PrEP Visits

Provider Checklist for Follow-up PrEP Visits

- ☐ **Brief counseling (every visit)**
 - Review/ask about signs and symptoms of acute HIV infection
 - Check on current context of sexual health
 - Desires to remain on PrEP
 - Facilitators & barriers to PrEP use
- ☐ **Adherence counseling (every visit)**
 - Monitor adherence (recall, pill count, etc.)
 - Brief adherence counseling
 - Discuss importance of effective use of PrEP
- ☐ **Assessment and management of side effects (every visit)**
 - Ask about and manage side-effects
- ☐ **Confirmation of HIV-negative status (recommended frequencies)**
 - Repeat HIV test one month after starting PrEP (especially if HIV RNA or antigen testing was not performed before starting PrEP)
 - Every three months thereafter
- ☐ **Calculation of estimated creatinine clearance (eGFR) (recommended frequencies)**
 - At least every six months
 - OR more frequently if there is history of conditions affecting the kidney (e.g., diabetes, hypertension, or any chronic nephropathy)
- ☐ **STI screening**
- ☐ **Risk reduction counseling**
 - Clients will be referred based on specific needs, i.e. social support, harm reduction, gender-based violence programs, etc.
- ☐ **Provision of condoms and lubricants**
- ☐ **Provision of contraception (as needed)**
 - Perform pregnancy test if needed
- ☐ **Provision of follow-up prescription for PrEP**
- ☐ **Scheduling of next appointment (provide appointment card)**

If a client using PrEP tests positive for HIV, stop PrEP and link promptly to treatment and care services. Start suppressive therapy for HIV infection (ART) immediately.

Please adapt this checklist to align with national guidelines on PrEP