Royal Government of Bhutan
Ministry of Health

Clinical Guideline for Pre-Exposure Prophylaxis for HIV Infection for Health Care Prescribers in Bhutan

Save the Children

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FOREWORD

In an era where the fight against HIV/AIDS continues to evolve, the development of effective prevention strategies becomes exigent. The emergence of PrEP as a cornerstone in our arsenal against HIV has transformed preventive strategies and improved the lives of countless individuals at risk of HIV infection. With its ability to reduce the risk of virus transmission by over 90% when taken consistently, PrEP offers a beacon of hope for those navigating the complexities of their sexual health and risk behaviors. However, the successful implementation of PrEP requires not only access to the medication but also clear and well-informed guidelines to ensure its proper use.

This guideline draws on the latest scientific evidence, best practices, and expert opinions to empower healthcare professionals across all levels of practice. By addressing critical components of PrEP implementation such as eligibility assessment, patient education, adherence strategies, and addressing potential barriers, we hope to equip providers with the tools necessary to facilitate informed decision-making for the provision of PrEP services.

As we introduce this guideline into clinical practice, we envision a future in which PrEP is not only recognized as a vital preventive tool but also as a standard component of comprehensive sexual health services. The ongoing commitment of healthcare providers, public health officials, and communities will be crucial in fostering a culture of prevention, support, and empowerment among individuals at risk of HIV.

This clinical guideline on Pre-Exposure Prophylaxis (PrEP) represents a significant milestone, as it is the first of its kind dedicated to providing comprehensive and evidence-based guidance to persons involved in providing PrEP in clinical and community settings in Bhutan. Doctors, Clinical Officers and Health Assistants who are the prescribers, Nurses, Laboratory and Pharmacy personnel, Counselors working in the clinical settings and peer outreach workers in the community setting will all be able to use this as clinical guide that gives an overview of how to provide Oral PrEP safely and effectively. We are excited to present this guideline as a foundational resource for those dedicated to making a meaningful impact in the fight against HIV/AIDS. Together, let us pave the way for a healthier, more informed world, where prevention is accessible, effective, and transformative.

Pemba Wangchuk

(Secretary)

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ABBREVIATIONS AND ACRONYMS

ADR	Adverse Drug Reactions	HIV	Human Immunodeficiency Virus
AGYW	Adolescent Girls and Young Women	HPV.	Human Papillomavirus
AHI	Acute HIV Infection	HRW	High Risk Women
AIDS	Acquired Immune Deficiency Virus	KPO	Key Population Organization
ART	Antiretroviral Therapy	PEP	Post-exposure prophylaxis
ARV	Antiretroviral	PrEP	Pre-Exposure Prophylaxis
CAB-LA	Long Acting Injectable Cabotegravir	PWID	People Who Inject Drugs
CBO.	Community Based Organization	PWUD	People Who Use Drugs
CSW	Commercial Sex Worker	RCDC	Royal Centre for Disease Control
CT	Chlamydia Trachomatis	RDT	Rapid Diagnostic Test
DSD	Differentiated Service Delivery	RFT	Renal Function Test
DVR	Dapivirine Vaginal Ring	SDC.	Serodiscordant Couples
EB-PrEP	Event-Based PrEP	STI	Sexually Transmitted Infection
ED-PrEP	Event- Driven PrEP	SW	Sex Worker
eGFR	Estimated Glomerular Filtration Rate	SUSARs	Suspected Unexpected Serious Adverse Reaction
ELISA	Enzyme-Linked Immunoassay	TAG	Technical Advisory Group
FTC	Emtricitabine	TDF	Tenofovir disoproxil fumarate

GC	Gonococci	TGM	Transgender Men
HBsAg	Hepatitis B Surface Antigen	TGP	Transgender People
HCV	Hepatitis C Virus	TGW	Transgender Women
HISC	Health Information & Service Center	TPHA	Treponema pallidum hemagglutination Assay
HIV-ST	HIV Self-Testing	WHO	World Health Organization

BACKGROUND

In 2015, WHO recommended offering oral PrEP containing tenofovir disoproxil fumarate (TDF) as part of the combination prevention package for people at substantial risk of acquiring HIV, such as men having sex with men, sex workers and transgender people adding to the arsenal of a combination of preventive measures for key population. By 2021, 144 countries adopted the WHO recommendations on oral PrEP in their national guidelines, with a further 14 countries with plans to adopt the recommendations by 2023. As per Global AIDS monitoring report 2024, the total number of people using oral PrEP has risen from a little over 200,000 in 2017 to about 3.5 million in 2023(18)

There is well established evidence both from systemic clinical trial research, real-life implementation research, and HIV programs that PrEP can have individual and population level benefits in growing optimism that pre-exposure prophylaxis (PrEP) reduces HIV incidence. PrEP has the potential to contribute to effective and safe HIV prevention when used in individuals at substantial risk for HIV acquisition and offers greater benefits when delivered as part of a comprehensive package of prevention services that include risk reduction and effective use counseling for using PrEP, access to condoms and lubricant, appropriate diagnosis and treatment of sexually transmitted infections(STIs), psychosocial support and monitoring of HIV status, side effects, and addressing additional risk behavior.

1. COUNTRY CONTEXT

Although Bhutan has a low HIV prevalence estimated at 0.2%, there is growing concern that the HIV epidemic is concentrated among the key populations and their partners. More than 82% of the reported HIV infections are attributed to heterosexual HIV transmission with approximately half of these cases associated to sex work. In Bhutan the estimated 97% of high-risk women exchanged sex for money and also reported the highest level of unprotected sex in the last 30 days (76%) [3]

Further, HIV prevalence among the subgroups of the key population was found to be higher than in the prevalence in the general population (3% in the female sex workers and 2% in the so-called "high risk women", 3% in among transgender people and 1.5% among MSM). It is a clear indication of the need to prioritize our interventions on the key populations and improve the quality and coverage of services for them and to address the barriers faced by them to access health services. It has been well recognized that there is a clear gap in HIV testing coverage for key populations.

Stigma and discrimination remain a critical barrier in people most affected by HIV to access services and is reflected in the gap in HIV testing coverage. The introduction of PrEP in Bhutan is an opportunity to strengthen HIV prevention services for men having sex with men (MSM), Transgender people (TG) and sex workers (SW), sero-discordant couples (SDC), especially where the partner living with HIV is not fully suppressed. Beyond the HIV prevention benefits PrEP is a gateway to provide sexual and reproductive health services, and especially relevant to sexually active adolescents and young people, pregnant and breastfeeding women as well as other vulnerable groups. It is also well recognized that PrEP can strengthen sexually transmitted infections (STI) management for both the key population and the broader general population through provision of asymptomatic STI testing e.g. *N. gonorrhoeae and C trachomatis* and appropriate treatment throughout the country.

1.1 Phased Implementation of PrEP in Bhutan.

Bhutan is taking the global and regional lessons from real-time PrEP implementation and adapted the WHO Differentiated Service Delivery (DSD) model for PrEP provision in the country's introduction and full-scale nation-wide rollout in 2026. The Principles of PrEP implementation is based on evidence, equity and putting people at the center of health care provision.

A. **Phase 1** will start in October 2024 in Thimphu and Paro Dzongkhag for key populations (MSM, TGP and Sex workers).
B. **Phase 2** will extend PrEP services to Chhukha and Sarpang Dzongkhags from April 2025, covering the same key populations along with PWID.
C. **Phase 3** will be a nationwide rollout of PrEP, anticipated to begin in January 2026. The experiences and learnings from Phases 1 and 2 will be systematically adapted and implemented in Phase 3 based on WHO's evidence -based recommendations on PrEP, and with a focus on strengthening differentiated service delivery and STI management.

Bhutan's approach to the initial phase of PrEP implementation is pragmatic. Outreach workers/community-based organizations (CBOs) will be central to the service delivery of PrEP; and in supporting people in navigating access to PrEP; from identifying prospective clients to linkage/referral to PrEP delivery points; further more outreach workers/CBOs will be enabled to get potential clients to initiate PrEP and stay on PrEP (e.g. assisted HIV self-testing; dispensation of PrEP medicine, client engagement/quality counseling to maximize effective use and retention when people using PrEP want to be maintained in services). The health facility-based PrEP services will be provided through the hospitals and HISCs.

2. DEFINING PrEP

a. WHO Recommended PrEP Products

In its latest recommendations, WHO recommends the following PrEP Products:

- Oral PrEP containing tenofovir, namely (tenofovir disoproxil fumarate (TDF) 300mg + emtricitabine (FTC) 200mg or TDF 300 mg + lamivudine (3TC) 300mg tablets)
- Dapivirine Vaginal Ring (DVR),
- Long acting injectable Cabotegravir (CAB-LA). All PrEP products are effective HIV prevention options.

In Bhutan Oral PrEP **Tenofovir Disoproxil\ fumarate (TDF) 300mg+Lamivudine (3TC) 300 mg, tablets** listed in the *National Essential Drug List 2021* will be used for PrEP. For oral PrEP there has been significant global scale up and is strongly recommended with high certainty evidence by WHO. For the other two WHO-recommended PrEP products (DVR and CAB-LA), experience with delivering them is largely restricted to clinical trials and research projects, and there are still significant gaps in clinical knowledge about delivering multiple PrEP products. Therefore, to start with only oral PrEP will be used but the other two can be offered as other choices in future when there is high certainty evidence of their use and when strongly recommended by WHO.

b. What is PrEP?

WHO defines Pre-exposure prophylaxis (PrEP) for HIV prevention as the use of antiretroviral (ARV) drugs by HIV-negative people to reduce the risk of acquisition of HIV? PrEP is recommended by WHO as an additional choice for people at substantial risk of HIV infection as part of combination prevention approaches.

c. How does PrEP Work?

When HIV enters the body, it infects the immune cells, multiplies within the cells, spreads throughout the body and continues to infect other immune cells, thus, destroying the immune system. PrEP, if taken consistently and correctly as per the prescription, the medication reaches an optimal level in the body and thus protects individuals from acquiring HIV infection after 7 days of daily dosing.

d. Who could benefit from PrEP?

HIV acquisition risk varies considerably within a person's sexual life, within populations and geographical locations. HIV population-level incidence is an important determinant of

individual-level risk of HIV acquisition. However, when considering who could benefit from PrEP, it is important to consider characteristics and behaviors of individuals and their partners that could lead to HIV exposures. Even in locations with low overall incidence of HIV, there may be individuals at substantial risk who could benefit from PrEP. The concept of risk is also very dynamic. People may 'enter' what is termed a 'season' or period of risk and that could be a period of just a few days, or longer periods. Vulnerable groups who may not always be able to negotiate HIV/STI prevention with their partners, including condom use due to power imbalances with sexual partners or are unable to negotiate because of drugs /alcohol use could also benefit from PrEP. In the PrEP literature and in the language of WHO, there is a trend to focus more on 'who could benefit" from prep as opposed to the branding of people or population as 'high risk' or 'at-risk' for HIV.

The following are persons would benefit from PrEP:

- Persons who recognize their own risk and request for PrEP
- Persons with more than one sexual partner.
- Persons who inject drugs (may also be at risk of sexual acquisition).
- Persons with recent STIs
- People who have been on PEP recently.
- People who do not use condoms consistently.
- Adolescent and young people.
- Sex workers
- MSM
- Transgender people
- Serodiscordant couples, particularly where the partner diagnosed with HIV is not virally suppressed.
- Pregnant and breast-feeding women.

3. COMPREHENSIVE SERVICE PACKAGE OFFERED WITH PrEP

The Comprehensive package has HIV rapid tests/ HIV self-testing will be part of the basic PrEP package for initiation/use; medical oversight in combination with this simplified PrEP delivery in Bhutan and a fixed dose combination of TDF+3TC will be used in Bhutan. PrEP as a gateway to strengthen STI management in Bhutan [including asymptomatic testing when resources are available]; syndromic case management until molecular testing becomes available [aligned to forthcoming *National STI guidelines in Bhutan*], will be part of the comprehensive package. The comprehensive service package for PrEP, if implemented to scale, can accelerate towards achievement of public health impacts such as reduction of the incidences of HIV, as well as improve case management of STIs including Hepatitis and thus safeguard the sexual and reproductive health of the general population.

The ongoing roll-out of HIV self-testing in Bhutan, coupled with PrEP introduction in October 2024, can create synergies in accelerating the closing of HIV testing gap, addressing stigma and discrimination in people most affected by HIV to access health services, and dealing with late detection of HIV cases for treatment initiation, delayed initiation of ART that constitute some of the major programmatic gaps in HIV response.

a. Minimum service package

A. Identifying HIV risk
B. Conducting HIV test (whether as an assisted HIV self-test or unassisted rapid HIV Test)
C. Assess for Post-exposure Prophylaxis (PEP)
D. Assess for signs of acute HIV infection (AHI)
E. Assess renal function.
F. Assess for contraindications to PrEP medicines.
G. Provide information on PrEP (effective use, side effects, how to engage with PrEP care team assigned to client) PrEP
H. Oral PrEP dispensed.

b. Additional services for oral PrEP

A. STI testing (syphilis, gonorrhea, chlamydia)
B. Hepatitis B surface antigen testing
C. HCV testing

D. Contraceptive services and Pregnancy testing
E. Prevention commodities such as condoms /lubricants/harm reduction services for PWID.
F. HBV vaccination for those born before 1997 and those born after 1997 who missed HBV vaccination.

4. PROCEDURES FOR PrEP INITIATION

As risk of HIV acquisition varies substantially between individuals, all clients must be assessed individually to identify persons with substantial risk of HIV acquisition (whether it has been ongoing, or people are about to enter a period of risk) and it is important to consider characteristics and behaviors of individuals and their partners that could lead to HIV exposure.

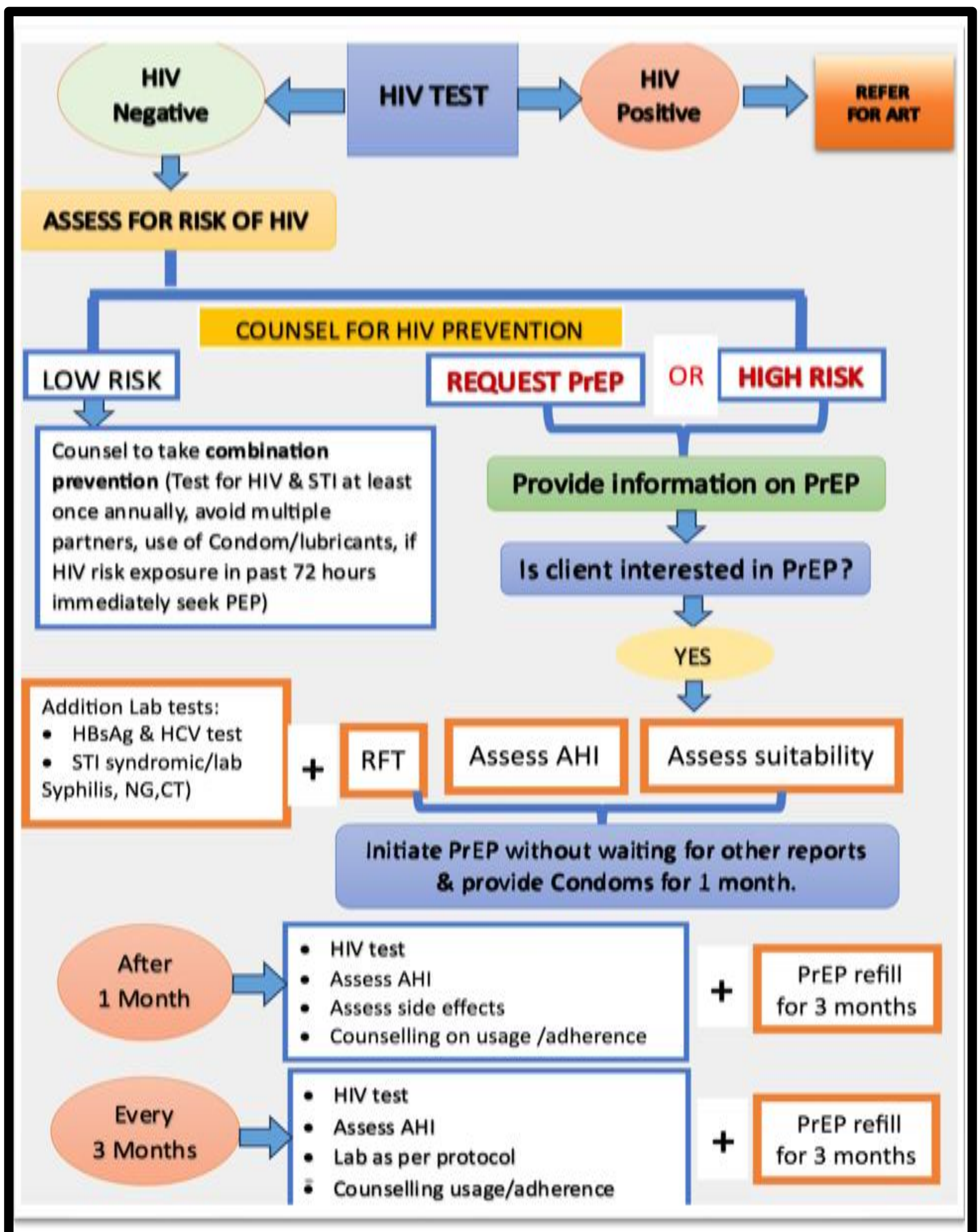


Figure 1. Algorithm for PrEP Initiation and Continuation

a. Identifying substantial risk of HIV acquisition

i. ASK ABOUT THE SEXUAL BEHAVIOR IN THE LAST 6 MONTHS

A. Condomless sex (anal or vaginal) with more than 1 partner with unknown HIV status?
B. Sex with an HIV positive partner? (Follow up with questions in Box 2)
C. Signs and symptoms / diagnosis of STIs?
D. Sex under the influence of drugs/alcohol?
E. Use of Post Exposure Prophylaxis (PEP)?
F. Self-perceived risk of HIV infection?
G. Ask if it is anticipated having condom less sex in the upcoming three months? *(E.g people may decide to 'drop' the condom when entering what they perceive as a monogamous relationship)*

If the person answers at least one "Yes" to the behaviors risk question above, the PrEP provider should discuss PrEP with focus on the benefits of PrEP even if the person has not specifically sought for PrEP.

ii. ASK MORE ABOUT HIV POSITIVE SEXUAL PARTNER

A. Whether an HIV positive partner is on ART for HIV.
B. Has the partner been on ART for more than 6 months?
C. If it is known when the partner had the viral load tested; if yes was the partner virally suppressed (was the viral load undetected).
D. Whether the partner is taking ART daily?
E. About desire / planning for pregnancy with the partner?
F. Ask about the usage of condoms every time they have sex.

b. HIV test

i. HIV SELF-TEST (HIVST)

It is used for the population at risk at the district hospitals, HISCs and at the community level. Outreach workers under Pride Bhutan and HISC are trained and certified to use HIVST and pre-test and post-test counseling. As per the existing protocol for the use of HIVST, the reactive cases are referred to the HISC and the non-reactive cases are linked to preventive services for HIV. HIVST done outside of a health facility will not be used for PrEP initiation and scheduled PrEP follow-ups. HIVST can be done in between scheduled PrEP visits to give assurance and confidence while on PrEP if the client wishes.

ii. Rapid Test (Antibody Testing)

It is conducted at all district hospitals and the 4th Generation ELISA test is conducted at RCDC (Regional Center for Disease Control) and JDWNRH.

c. Baseline HIV Testing for PrEP Initiation

For PrEP initiation in Bhutan two tests will be performed at baseline (a rapid antibody test and a 4th generation ELISA simultaneously). The hospitals will collect two samples of blood and conduct a rapid test and send one sample to Thimphu (JDWNRH /RCDC) where the 4th generation test is available. A 4th generation test will be mandatory for initiation of PrEP.

- **If Rapid Test is Reactive:** Follow the National Guideline on Treatment of HIV-AIDS 2024 for HIV testing and management.
- **If Rapid Test is Non-reactive:** Assess for potential HIV risk exposure in the last 72 hours or 14 days before onset of the AHI as per the HIV Testing algorithm for PrEP initiation and continuation (Figure 2). If high risk exposures are excluded and rapid HIV is non-reactive, initiate PrEP without waiting for the 4th generation ELISA test results.
- If the 4th generation test result comes out positive, stop PrEP immediately and refer the client for immediate ART.

d. HIV testing for PrEP continuation

- Follow up with HIV Rapid test (Antibody testing) for follow up at 1 month, 3 month and 6 months.
- Thereafter, follow up with alternative self-testing and rapid testing every 3 months (ie: self-testing at 9th month, rapid testing at 12th month) till the time the individual continues to take PREP.

e. Assessing for PEP

PEP is the use of ARVs by HIV negative individuals to prevent acquisition of HIV after a possible HIV exposure. People who come for PrEP services may have had an exposure within the previous 72 hours (condomless sex with more than 1 partner or HIV positive partner, breakage of condom during sex, injecting drug use with shared injection equipment) or if a client on PrEP has not adhered to PrEP within the past 72 hours non- occupational post - exposure prophylaxis (nPEP) as per the National PEP guideline should be immediately started and used for 28 days.

At the end of the 28 days if the client tests negative for HIV, PrEP can be started after all procedures for PrEP initiation are repeated, even without a gap, more so if the client has ongoing HIV risk.

PEP is most effective when taken within 24 hours after an exposure and should be started as soon as possible.

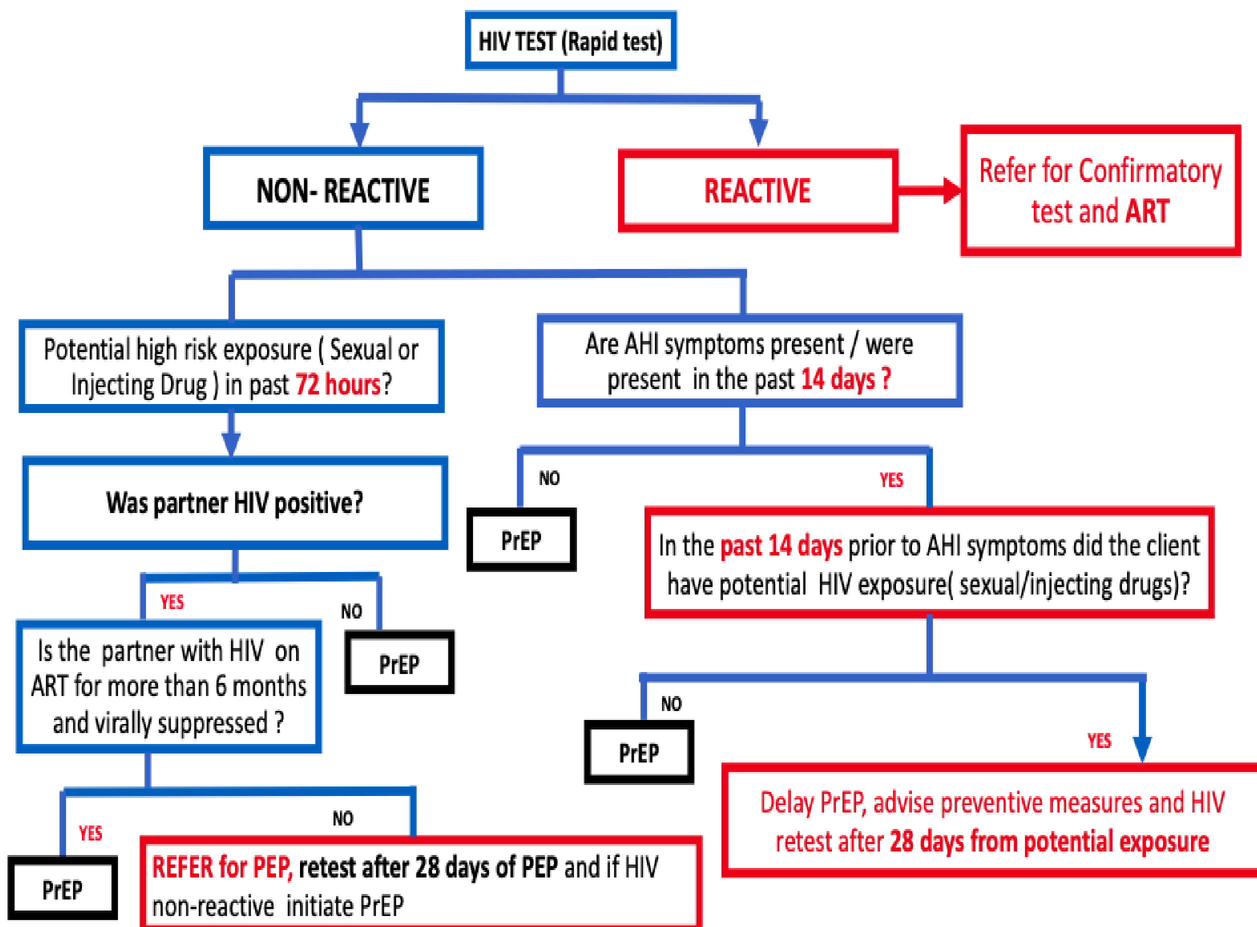


Figure 2. Algorithm for HIV Rapid Test to Assess PEP and AHI

f. Assessment for signs and symptoms of AHI.

To minimize the risk of drug resistance, the likelihood of AHI should be assessed for all individuals starting oral PrEP and also those who are on PrEP for effective use of PrEP. If AHI signs and symptoms are present, the client should be assessed for possible recent exposure to HIV within the last 14 days. If high risk exposure is found withhold PrEP and provide other preventive measures and retest after 4 weeks of the potential risk exposure. If a PrEP provider concludes that the exposure is low risk and a clinical judgment should be made and PrEP can be initiated as per the procedure for initiating PrEP.

g. Assess for Contraindications

The client should be assessed for contraindications to the oral PrEP regimen. If the client has hypersensitivity or allergies, they should be offered alternative prevention options.

i. Contraindications For PrEP

A. HIV Positive
B. High HIV risk exposure within the past 72 hours.
C. Suspected acute HIV infection (AHI) with a potential HIV exposure in the previous 14 days
D. Allergy or hypersensitivity to the PrEP product.
E. Persons with abnormal renal function tests. (Creatinine clearance below 60 mL/min)

h. Suitability for PrEP

i. Clinical Suitability for PrEP

A. Age > 15 years (weight >35 Kg)
B. HIV-negative
C. No symptoms of acute HIV infection symptoms
D. No contraindications to PrEP medicines (e.g., TDF/3TC)
E. Willingness to use PrEP as prescribed
F. Willingness to take periodic HIV testing and follow-up visits

i. Baseline Laboratory Procedures

Following a negative HIV test and the person confirms that they are interested in taking PrEP, baseline investigations should be conducted before PrEP can be initiated (refer to Table 1).

Table 1. Baseline Laboratory procedures to be performed prior to initiating a client on PrEP

Procedures	Priority actions
HIV testing	Based on the findings from behavioral risk assessment and a **non-reactive result for the first test in the national algorithm, start PrEP without waiting for the 4th generation ELISA test result.**
Renal function test (Serum creatinine clearance) *	• **RFT reports need not be available prior to starting PrEP.** • If eGFR < 60ml/min DO NOT initiate PrEP, repeat in 2 weeks and if eGFR > 60 ml/min start PrEP. • If the Renal function test is abnormal, the client should be contacted immediately and told to stop PrEP immediately.
Hepatitis B surface antigen (HBsAg)	• **Results of the HBsAg test need not be available prior to starting PrEP.** • If HBsAg -ve : start PrEP and vaccination for those born before 1997 and those who have missed if born after 1997. • If HBsAg Positive: start PrEP and refer to the doctor /specialist for management of Hepatitis B.
Hepatitis C Antibody tests (anti-HCV)	• **Result of HCV test need not be available prior to starting PrEP.** • If HCV -ve: start PrEP • If HCV +ve : start PrEP and refer to the doctor /specialist for management of HCV infection.
STI (Syndromic or Laboratory for syphilis, Swab for GC, CT)	• Syndromic management • For syphilis TPHA as first line testing till HISC. • Swab for GC will be done at hospital settings only. • Asymptomatic testing for CT and GC if made available later on. • If STI diagnosed, provide treatment for STI based on the National STI Guidelines 2024.

Pregnancy testing and contraceptive services	Assess reproductive intentions and offer pregnancy testing, if appropriate and reliable contraception.

**Note: Known kidney impairment (indicated by an estimated glomerular filtration rate (eGFR) of under 60mL/min per 1.73m2 or a creatinine clearance of less than 60mL/min) is a for TDF-based oral PrEP.*

j. PrEP Follow Up and Monitoring

- Clients must return at month one and every three months for follow-up HIV testing, safety monitoring.
- These schedules can be adapted to the client's needs and preferences. For example, a client using oral PrEP may be traveling for extended periods of time (and so may not be able to meet a suggested visit schedule), so the client can make unscheduled visits for anything regarding PrEP that concerns the client.
- Test for HIV (only clients who have a negative test result should continue PrEP)
- HIV self-testing (HIVST) may be appropriate for people using oral PrEP between scheduled PrEP visits to give reassurance and confidence.
- Check-in with the client (for example, discuss sexual health concerns and goals, key messages about PrEP, side-effects and intention to continue PrEP).
- Assess for effective use of PrEP (assess for AHI and PEP if PrEP use was not effective).
- Provide (or refer for) any of the suggested additional services appropriate to the PrEP product and client, for example, STI screening.

k. Key messages

- PrEP is effective if used as prescribed during periods of HIV risk.
- PrEP does not offer prevention against other STIs or pregnancy.
- PrEP, generally, is safe and well tolerated. Side effects are typically mild and resolved on their own and can be treated symptomatically.
- Severe side-effects should be reported to your PrEP provider (or anyone on your designated PrEP care team) without delay.
- Regular follow up is important to support effective PrEP use and to avail other services including STI and HIV.
- Only the results of an HIV test are required to continue PrEP. Refer Table 2 for follow-up procedures.

Table 2. Procedures for PrEP Initiation and Follow-up

	Procedures	**Month**					
		0	**1**	**3**	**6**	**9**	**12**
1	HIV test (baseline and 3 monthly)	×	×	×	×	×	×
2	Assess for PEP (baseline and every visit)	×	×	×	×	×	×
3	Assess for AHI (baseline and every visit)	×	×	×	×	×	×
4	Assess for contraindications	×					
5	Provide oral PrEP (month 1 then 3 monthly refill)	×	×	×	×	×	×
6	Renal function test (baseline, at Month 3 and then 6 monthly)	×		×		×	
7	STI Testing (Baseline and 6 monthly)	×			×		×
8	Hepatitis B surface antigen testing (Baseline and then annually)	×					
9	Hepatitis C antibody testing (Baseline and then annually)	×					

10	Counseling (effective use, side effects, successes and challenges) every visit	×	×	×	×	×	×
11	Preventive measures (condoms/lubes/NSP) every visit.	×	×	×	×	×	×
12	Pregnancy testing and contraception (if needed)						
13	HBV vaccination for those born after 1997 who have not been vaccinated and those born before 1997						
14	PrEP medication issuance	×	×	×	×	×	×
15	Behavioral sexual risk reduction counseling	×	×	×	×	×	×

5. PRESCRIPTION OF PrEP DRUGS

a. Dosing Regimens and Management of Oral PrEP

- There are currently two dosing regimens for TDF-based oral PrEP:
    - **Daily PrEP**: Daily PrEP, also called daily dosing, refers to taking one dose of oral PrEP every day over a period. For details on how to start or stop oral PrEP safely and effectively, refer to the population specific guidance outlined in this guideline.
    - **Event-Driven or Event-based PrEP (ED PrEP or EB PrEP)**
- Irrespective of the dosing regimen, everyone should be **empowered** to safely start, continue, stop and restart oral PrEP.
- There is no time limit on how long a client can take oral PrEP, nor on the number of times a client can restart oral PrEP**.**
- Daily PrEP is suitable for all people who are at risk of HIV.
- Daily PrEP is the only regimen that is recommended for PWID and people with chronic Hepatitis B.
- **Daily PrEP is the only suitable regimen for Cis-gender MSM with chronic hepatitis B infection** to maintain virological suppression, prevent drug resistance and hepatitis flare.
- Only Cis-gender MSM can choose between daily PrEP and ED PrEP.
- MSM may choose EB-PrEP if they have side effects while using daily PrEP or have poor renal functions.
- ED-PrEP is preferential for those MSM who:
    - Who can plan for sex at least 2 hours in advance
    - Who can delay sex for at least 2 hours.
    - Who have sex less than twice a week.
- If an individual **misses a dose, they should take it as soon as they remember**; but should not take more than two doses in one day.
- If an individual stops taking PrEP (specifically, has **more than two days without taking a dose),** the next time they anticipate having sex or want to restart oral PrEP, they **should start the regimen all over again.**

Table 3. Prescription of PrEP

Population	Type of dosage regime	Starting	Using	Stopping
For all other groups	Daily Oral PrEP	Take one dose per day for day for seven days prior to exposure;	Take one dose per day during exposure;	Continue with one dose per day for seven days after the last exposure. (Refer figure 6-1)
For all individuals assigned male at birth with sexual exposure and NOT taking gender affirming hormones[1]	Event Driven or Event based PrEP	Take two doses 2-24 hours prior to exposure;	Take one dose per day during exposure;	Continue with one dose per day for two days after the last exposure. (Refer figure6-2)

[1] *Cisgender men and transgender women **not** taking gender-affirming hormones can adapt PrEP use to their HIV*

prevention needs and preferences. Some people may use PrEP for a single event (for example, sex on only one day), or for infrequent "single" events that are weeks or months apart. This is sometimes called event-driven PrEP (ED-PrEP) or 2+1+1.

A. Example oral PrEP dosing regimen for all other groups, including cisgender women, transgender women (taking gender affirming hormones) and people who inject drugs

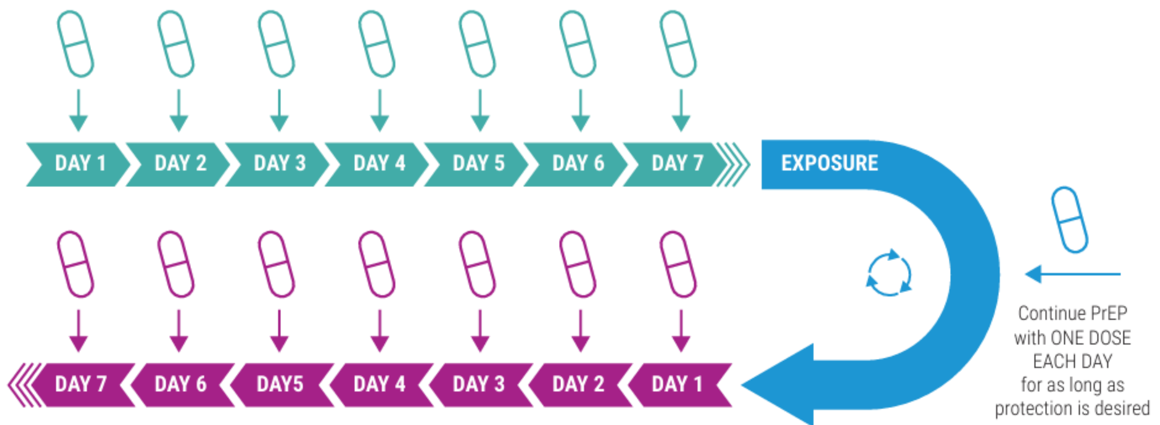
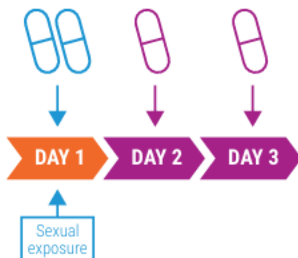


Figure 3. Daily Oral PrEP dosing regimen

B. Example oral PrEP dosing regimen for cisgender men and transgender women (not taking gender affirming hormones) with sexual exposure

PrEP for a single event e.g. sex on 1 day



PrEP for multiple events or daily

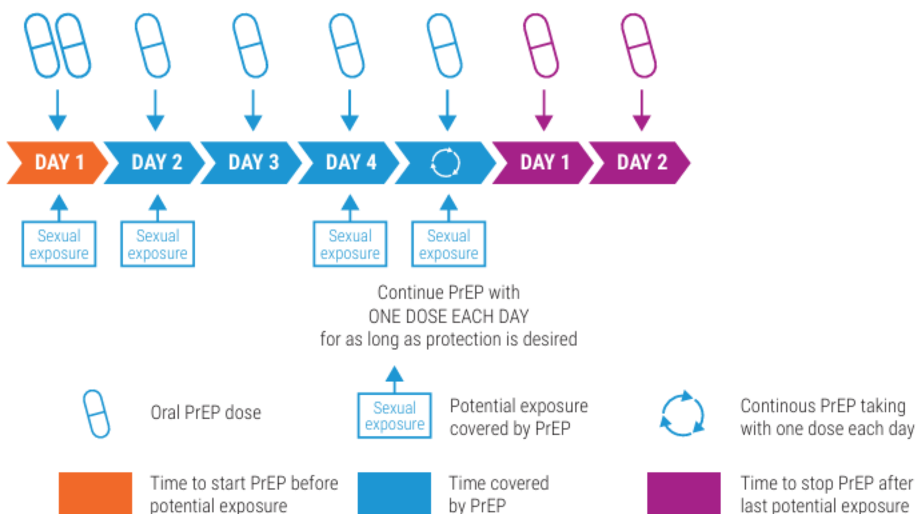


Figure 4. Event- driven Oral PrEP Regimen

6. STOPPING AND RESTARTING PrEP

a. Stopping PrEP

- PrEP should be stopped if the client:
  - Tests HIV-positive
  - Develops renal disease
  - Is non-adherent to PrEP
  - No longer needs or wants PrEP
  - No longer meets eligibility criteria
  - If there are safety concerns where the risks of PrEP use outweigh potential benefit
  - Clients may have chosen to use an alternative HIV prevention method.
  - No longer perceive themselves at risk of HIV. When an HIV sexual partner achieves sustained viral suppression after at least 6 months of ART.
  - When a client enters a mutually monogamous relationship with a sero-discordant partner. When other social circumstances change.
- PrEP providers should help clients assess their prevention needs and exposure to HIV, but clients should not be required to return to a PrEP provider to stop PrEP if they know how to stop. If a client wants to discontinue using PrEP for any reason, the client should come to the PrEP Provider to complete exit formalities.
- Clients should be informed about how to safely stop PrEP, emphasizing the need to continue PrEP for the recommended time after their last potential HIV exposure.

b. Restarting PrEP

- Reasons for restarting PrEP may be:
  - Traveling to locations with high prevalence /unknown prevalence of HIV during which they anticipate having condom less sex with casual partners or using injectable drugs.
  - Starting a new relationship with an HIV-positive partner who is not on ART or with unknown HIV status.
  - Starting or restarting sex work
  - Entering a period of engaging in condom less sex.
  - Leaving a long-term relationship.

- Clients who have stopped oral PrEP, can restart PrEP using the dosing regimen suitable for them.
- When restarting the same PrEP choice, PrEP providers should use a similar approach as was used when they first initiated PrEP.
- Individuals should always be tested for HIV prior to restart PrEP as per the HIV testing Protocol for initiation of PrEP even if the last test was less than three months earlier and also assess for contraindications.
- Some of the additional tests may not be repeated if results are available and if they have been conducted within an appropriate time frame as per the testing schedule for PrEP follow-up

7. POSSIBLE SIDE-EFFECTS AND ADVERSE DRUG REACTION

PrEP (TDF /3TC) has a good safety profile. Possible side-effects of oral PrEP are usually mild and may be experienced by 1 in 10 PrEP users. Side-effects such as nausea, abdominal cramps, headache; these are usually mild and resolved over the first month of taking PrEP. 1 in 200 may have creatinine elevation (typically reversible after stopping PrEP). And rare side effects reported is loss of bone mineral density that recovers after stopping PrEP.

Adverse Drug Reaction may be considered when:

- It results in death or is life-threatening.
- The condition requires in-patient hospitalization.
- It results in some sort of disability.

a. Reporting of ADR

- Adverse Drug reaction will be reported to TAG within 24 hours
- Fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs) also need to be reported to TAG within 7 days.
- Non-fatal life-threatening SUSARs to be reported to TAG within 15 days.

b. Documentation of Adverse Drug Reaction

If a serious side effect is observed, it must be reported in detail to ensure client safety as follows:

- Follow the ADR reporting as per the existing policy and for PrEP follow the additional following steps.
- All documents (behavioral risk assessment, clinical suitability assessments, and laboratory results) must be filed properly in the client's file with all forms and client notes and kept safely.
- All serious side effects must be clinically evaluated to determine if it is drug related.
- If minor side effects are reported symptomatic management can be given and separate reporting is not needed.
- Any event before a client is enrolled must be documented as medical history.
- The PrEP providers assess the problem based on the vital signs and laboratory reports and follow up such cases until the problem is resolved.

8. ASSESSMENT FOR CONTRAINDICATIONS AND DRUG-INTERACTIONS

- Oral PrEP can be taken with or without food.
- Oral PrEP does not have any known interactions with contraceptive hormones and does not affect levels of estradiol-based exogenous (gender-affirming) hormones used by transgender individuals.
- Oral PrEP does not have interactions with most used medicines and can be safely taken at the same time as antidepressants, tuberculosis (TB) and/or malaria medicines.
- There is no evidence that taking alcohol or recreational drugs such as heroin and other opioids, cocaine or methamphetamine concurrently with oral PrEP reduces the effectiveness of oral PrEP.
- For some people, excessive use of alcohol or recreational drugs may impede their ability to take oral PrEP as recommended, and PrEP providers should counsel and support people on effective use.

a. Special situations

- PrEP is safe for use in pregnant or breastfeeding women who are at substantial risk of HIV acquisition.
- In serodiscordant relationships PrEP can be safely used by the HIV negative partner. In serodiscordant couples, PrEP has provided a useful bridge for the HIV-negative partner until full viral suppression of partner with HIV is reached. PrEP can protect an HIV-negative person in a serodiscordant relationship when the partner living with HIV is either not on ART or is not virally suppressed.
- People who inject drugs are at substantial risk of acquisition of HIV and should be provided with a package of effective HIV services such as harm reduction services such as Needle and Syringe program (NSP) that are the mainstay of HIV prevention.
- PrEP can be considered for people who use drugs in particular, among people who use amphetamine type stimulants and engage in higher risk sexual practices (including among some subgroups of men who have sex with men in some settings). There may also be a link with sex work, and they may not be able to use condoms effectively with all clients or with intimate partners. They should be provided with a package of effective HIV services such as condoms besides the prevention package relevant for drug use.

PWUD in particular amphetamine type stimulants and engage in higher risk sexual practices may not be able to use condoms consistently with all clients or with intimate partners.

9. Ensuring Effective use

- Effective use is important to prevent HIV acquisition (this means using PrEP according to the dosing schedule during periods of HIV risk).
- PrEP is effective but when used as part of the combination prevention package for people at substantial risk of acquiring HIV, it is almost 99.9% effective.
- Regular follow-up is important to support effective PrEP use and to provide other services including follow-up HIV testing and safety
- PrEP providers can assess effective use at each visit by discussing possible HIV exposures and PrEP use (including any missed doses).
- To be effective, all possible exposures should be covered by PrEP.
- Clients should be assessed for PEP, and AHI considered, if there has been ineffective use of PrEP (specifically, missed doses around the time of possible HIV exposure).
- If a client reports challenges with effective use of PrEP, healthcare providers should help their clients to identify a range of strategies to make effective use easier.
- PrEP is not a lifelong commitment. People using PrEP can generally stop, start and restart PrEP as their needs and circumstances change.
- PrEP providers should empower clients to use PrEP effectively, including appropriate starting, stopping and restarting.
- PrEP providers should support clients who want to switch from ED-PrEP to Daily PrEP and vise-versa and provide information about how to do this safely and effectively.
- If clients want to switch the dosing regimen they have to report and consult with the PrEP Provider.
- Oral PrEP is safe during pregnancy and breastfeeding.
- If a pill on that day it should be taken as soon as the client remembers it the same day.
- If the client does not remember till the next day, 2 pills should not be taken on the same day, just take one pill as usual.
- If the client is cisgender man on daily PrEP (with sexual exposure) who misses 3 doses in the past 7 days, PrEP should be stopped immediately and PEP should be considered.
- For all clients (except cisgender men) on daily PrEP (with any type HIV exposure risk) who missed 5 doses in the past 7 days, PrEP should be discontinued and PEP should be considered (10).

***Adolescents, people who used drugs and alcohol*: may benefit from more frequent appointments e.g. monthly visits to address changing routines and multiple needs.**

10. Management of creatinine elevation

- Approximately 80% of creatinine elevations are self-limiting (without stopping PrEP) and resolve when a separate specimen, collected on a different day, is tested.
- Creatinine elevations associated with starting PrEP usually reverse after stopping PrEP.
- If the creatinine elevation is confirmed on a separate specimen and if the **estimated creatinine clearance decreases to less than 60 ml/min,** consider discontinuing PrEP.
- **Once PrEP is stopped, creatinine levels can be rechecked one to three months later and PrEP can be restarted if renal function returns to more than 60 ml/min.**
- Additional causes and management of creatinine elevations can be considered, especially if any of the following are present:
  - Creatinine elevations are more than 1.5-fold the upper limit of normal.
  - Renal function or creatinine elevations do not return to normal levels within three months of stopping PrEP;
- Creatinine elevations progress at one month or more after stopping PrEP

11. Management of seroconversion

- HIV seroconversion may occur after initiating PrEP.
- Reasons for Sero-conversion can be:
  - Due to HIV infection that was there while starting PrEP.
  - Due to ineffective use of PrEP /poor adherence to PrEP.
- Confirm reactive rapid test results according to the national testing algorithm and start ART immediately.

If a PrEP user has a confirmed HIV diagnosis at follow-up, PrEP should be immediately discontinued and client to be referred for ART.

Seroconversion should be reported to TAG within 24 hours.

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ANNEXURE: COUNSELING CHECKLISTS

Table 4. Prep Initiation Patient Counseling Checklist

PrEP INITIATION PATIENT COUNSELING CHECKLIST	
"I have discussed all these points with the client"	
1. Their risk of acquiring HIV and the benefits of PrEP	
● When taken appropriately PrEP offers more protection against HIV than condoms (PrEP around 99% vs 90% condoms)	
● PrEP is an optional medication used to prevent HIV that will require taking medication responsibly.	
2. Information about Oral PrEP and to start, use and stop oral PrEP and restarting.	
● PrEP can be started and stopped at any time based on the patient's preference and risk (the HBV status should be kept in mind)	
● Side effects: Oral PrEP is well tolerated with common side effects such as abdominal cramps, nausea, headache which may be mild, non-life threatening and resolve on its own within the first month of taking PrEP occurring in 1 in 10 persons only.	
● If side effects do not go away and it makes you too sick, please contact the PreP Provider but do not stop taking PrEP until you see the PrEP provider.	
3. Starting and Stopping PrEP	
● PrEP takes time to reach adequate levels in blood to provide protection. ● For daily Oral PrEP : 7 days of consecutive use is required **before sex** then take daily till there is exposure and if you want to stop take 7 more days **after the last sexual activity.** ● For ED-PrEP 2 pills 2-24 hours **before sex** and 1 pill every 24 hours for 48 hours **after last sexual activity.**	

4. Why it is important to use condoms

- When you start PrEP, till you achieve full protection, condoms should be used for additional protection.
- PrEP does not protect against STIs
- Inform to use Barrier methods (Condom) and routine STI testing at baseline and every 6 months
- PrEP does not protect against pregnancy
- Discuss about options for contraception and family planning
- Even if you forget to take PrEP sometimes, if you used condoms you are protected on those days.

5. Restarting PrEP

- If you stopped PrEP and want to restart after a gap *HIV test must be done before you restart*. Contact the PrEP provider and the process of initiation of PrEP must be repeated to ensure you are HIV negative when you restart PrEP.

6. PrEP use must be monitored along with HIV testing as per the follow-up schedule

- For oral PrEP follow up schedule is at month 1 and then every 3 monthly and you must report to the PrEP site for the scheduled follow up.
- Unscheduled visits can be made anytime between the scheduled vivists in case of any problems like side effects, pills loss, etc.

7. About PrEP medication and what to do if you miss PrEP

- Pills should be kept out of reach of children
- Stored away from sunlight and moisture
- Pills prescribed for you cannot be shared to others as anyone who takes PrEP has to be checked if they are suitable to take PrEP.
- Pills should be taken at a convenient time preferably at the same time of the day.

- If you miss a pill on that day, you should take it as soon as you remember it the same day.
- If you do not remember until the next day, do not take 2 pills on the same day, just take one pill as usual.
- If a cisgender man who is on daily PrEP (with sexual exposure risk) missed 3 doses in the last 7 days, PrEP should be discontinued immediately and PEP should be considered.
- All other groups on daily PrEP (except cisgender men) with any sort of HIV risk exposure(Sexual or Injecting drug use) missed 5 doses in the last 7 days, PrEP should be discontinued immediately and PEP should be considered.
- If you have problems with side effects that do not subside, or you need to ask anything about PrEP use you are welcome to contact me at. (Contact No ……………………….of PrEP provider.)

Table 5. PrEP Continuation Patient Counseling Checklist

PrEP CONTINUATION PATIENT COUNSELING CHECKLIST
"I have discussed all these points with the client"
1. Review any issues with getting services for PrEP 2. Assess for side effects and any other concerns 3. Discuss adherence: reasons for missed doses and strategies to improve adherence 4. Review continuing risk factors and provide risk reduction strategies. 5. Reinforce the point that PrEP does not protect against STIs or prevent pregnancy 6. Review lab reports and discuss related management 7. Discuss about other aspects of Primary health care if any.

Table 6. Prep Discontinuation Patient Counseling Checklist

PrEP DISCONTINUATION PATIENT COUNSELING CHECKLIST
"I have discussed all these points with the client"
1. Document the reasons why the person wishes to stop PrEP 2. Ensure that the person is not HBsAg positive as discontinuation may potentially lead to hepatitis flares. 3. Retest for HIV and STIs, Pregnancy test if applicable. 4. Encourage barrier methods, routine testing and risk reduction strategies if the patient continues to engage in high-risk sex and /or IVDU. 5. Inform the person that PrEP can be restarted whenever the patient enters a HIV risk situation. 6. Protection from oral PrEP will wane **after a week.**

Table 7. HIV Seroconversion while on PrEP Patient Counseling Checklist

HIV SEROCONVERSION WHILE ON PREP PATIENT COUNSELING CHECKLIST
"I have discussed all these points with the client"
1. Allow patients the time needed to express their emotions which may range from grief to anger. 2. Ask the patient their understanding of what contracting HIV means 3. Without disregarding these emotions, mindfully explain that HIV is no longer a "death sentence" 4. Very effective treatment options exist that allow for normal life expectancy. ● Care for HIV will be very similar to their care during PrEP. ● Current treatment options can achieve undetectable viral loads in a matter of months. This is called a "functional cure," and eliminates nearly all of the harmful impacts HIV causes on the body. 5. HIV is a chronic condition that is best controlled with medication adherence. ● Eliminate stigma associated with the diagnosis. ● Explain about other chronic conditions (diabetes, hypertension, dyslipidemia) that are also usually lifelong diseases that require daily medication use. They are no different. 6. Explain that notifying potential exposures (especially those in the past 72 hours for non-occupational PEP purposes) is important to limit communal spread BUT reassure patients that anonymous reporting is an option. 7. Refer patients to comprehensive care: HIV services, therapy, case management, etc.

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