GUIDELINES

FOR THE PROVISION OF PRE-EXPOSURE PROPHYLAXIS (PrEP) TO PERSONS AT SUBSTANTIAL RISK OF HIV INFECTION

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ABBREVIATIONS AND ACRONYMS

AGYW	Adolescent girls and young women
ART	Antiretroviral therapy
ARV	Antiretroviral
FTC	Emtricitabine
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
HTS	HIV testing services
M&E	Monitoring and evaluation
MSM	Men who have sex with men
NDoH	National Department of Health
PEP	Post exposure prophylaxis
PrEP	Pre-exposure prophylaxis
SRH	Sexual and reproductive health
STI	Sexually transmitted infection
SW	Sex worker
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TDF/FTC	Tenofovir disoproxil fumarate/Emtricitabine
WHO	World Health Organization

Term	Working definitions in these guidelines
AGYW	Adolescent girls and young women aged 15 to 24 years.
Adult	Person older than 19 years.
ART	Antiretroviral therapy refers to the use of a combination of three ARV drugs to achieve viral suppression and is given for life.
ARV	Antiretroviral drugs refer to the medicines active against HIV.
Combination HIV prevention	A combination of behavioural, biomedical, and structural approaches to HIV prevention to achieve maximum impact on reducing HIV transmission and acquisition.
Healthcare provider	Anyone who renders healthcare; includes doctors, nurses, pharmacists, trained counsellors, and community health workers.
PEP	The preventive ARV medical treatment started within 72 hours after exposure to HIV to prevent infection.
PrEP	The use of antiretroviral drugs by HIV-negative people before potential exposure to prevent the acquisition of HIV.
Serodiscordant couples	Couples in an ongoing sexual relationship in which one partner is HIV-positive and the other is HIV-negative.
Sex worker	Women, men, and transgendered people of all ages, who receive money or goods in exchange for sexual services, and who consciously define those activities as income generating even if they do not consider sex work as their occupation.
Substantial risk	Substantial risk of HIV infection is defined as a population group with an HIV incidence greater than 3 per 100 person-years in the absence of PrEP.
Young women	Women aged 20 to 24 years, inclusive.

1. INTRODUCTION AND BACKGROUND

South Africa has the largest HIV epidemic in the world, with 7.9 million people aged 15 to 49 living with HIV in 2017, representing 19% of the global HIV burden. As of 2018, there were just over 4.4 million people in South Africa on antiretroviral treatment (ART), which is the largest ART programme in the world. Despite this accelerated progress and the introduction of Test and Treat All in 2016, there were approximately 231 000 new HIV infections in 2017. [1]

The HIV epidemic varies significantly across and within different geographies in South Africa. Even though the epidemic is generalised, it is over-represented in some populations, including sex workers (SW) and men who have sex with men (MSM). It is also concentrated in the populations with very high vulnerability to HIV, such as adolescent girls and young women (AGYW). This contextual understanding of the HIV epidemic is critical to develop and implement effective HIV interventions. Differential vulnerability levels, social risk factors, high-risk sexual practices, and limited access to appropriate HIV interventions influence HIV incidence among these populations.[2,3,4]

WHO recommends supporting and strengthening primary HIV prevention alongside treatment, as both are needed to meet the 90-90-90 targets. In 2015, WHO recommended that all HIV positive people should be offered antiretroviral therapy (ART), regardless of their CD4 count and clinical staging, which will prevent both horizontal and vertical transmission of HIV. WHO also issued a strong recommendation that HIV negative people at a substantial risk of HIV infection should be offered daily oral HIV pre-exposure prophylaxis (PrEP) as part of a combined HIV prevention strategy. This recommendation enables a wider range of populations and individuals to benefit from this additional prevention option and is based on individual risk assessment. PrEP however, should not replace or compete with effective and well-established HIV prevention interventions, such as condom use.[5]

These guidelines focus on the provision of PrEP as part of comprehensive combination prevention, drawing on implementation and research evidence and WHO recommendations.

Access: Identify individuals at highest risk of HIV and ensure access to HIV prevention interventions, including PrEP.

Integration: Integrate PrEP into other HIV prevention programmes including sexual and reproductive health services.

Quality of care: Provide PrEP within broader framework of quality health service provision.

Public health and rights-based approach: PrEP can enable and empower individuals to have an informed choice of HIV prevention options, using a public health approach. This includes confidentiality, access to non-discriminatory healthcare, privacy, choice, informed decision-making, and shared responsibility.

3. DEFINING PrEP

3.1. What is PrEP?

PrEP is defined by the WHO as the use of antiretroviral drugs by HIV-negative people who are at substantial risk of acquiring HIV before potential exposure to HIV to prevent HIV acquisition. It is an evidence-based HIV risk-reduction intervention. Substantial risk is defined as an HIV incidence greater than 3 per 100 person-years in the absence of PrEP.[5] The current preferred regimen in South Africa is oral TDF/FTC as a fixed-dose combination.

3.2. PrEP, PEP and ART

Pre-Exposure Prophylaxis (PrEP)	Post-Exposure Prophylaxis (PEP)	Anti-retroviral treatment (ART)
ARV medication taken by HIV-negative persons before exposure to HIV to prevent HIV acquisition	ARV medication taken within 72 hours after exposure to HIV and continued for 28 days to prevent HIV acquisition	Lifelong treatment with ARV drugs for people with HIV to minimize the effect of HIV by increasing the CD4 count and reducing the viral load

3.3. Identifying Potential Candidates for PrEP

Identifying people at substantial risk of HIV infection who may benefit from PrEP and are willing to take PrEP; or who may, with assistance, be motivated to continue with PrEP is essential for programme efficiency.

Specific populations considered to be at substantial risk of HIV infection include:

- Adolescent girls and young women
- Men who have sex with men
- People more than one sexual partner
- People who inject drugs
- People with a recent history of STI(s)
- People who recognise their own risk and request PrEP
- Serodiscordant couples if the HIV positive partner is not virally suppressed
- Sex workers

3.4. Minimum Package of Services Offered with PrEP

PrEP must be integrated into existing sexual and reproductive health services and should not be offered as a vertical programme. The following minimum package of services must be provided to all clients receiving PrEP services in accordance with national guidelines:

- HIV Testing Services
- ART initiation for those diagnosed with HIV
- Syndromic STI diagnosis and treatment
- Condoms and Lubricants
- Pregnancy screening
- Contraception
- Counselling for Mental Health
- TB Screening

4. PROVISION OF PrEP

4.1. Screening for PrEP

A set of risk assessment questions have been developed to assist in differentiating individuals at substantial risk of HIV infection from those who are not.

HIV negative individuals who answer “yes” to any of the following questions should prompt a discussion about the risks and benefits of PrEP.

A person requesting PrEP must always be considered.

In the recent past or last six months:	**A client in a serodiscordant relationship:**
• Have you had sex without a condom? • Have you had sex without a condom with an individual whose HIV status did not know? • Have you had an STI? • Have you had sex with more than one partner without a condom? • Have you had sex under the influence of alcohol and/or drugs?	Have you had sex with a person who has HIV? (if yes ask below questions) • Is your partner taking ART? • If yes to above is it for more than 6 months? • Do you know if your partner is virally suppressed? • When was the last viral load test done? • Do you desire to have a baby with your partner? • Do you use condoms every time you have sex?

4.2. Eligibility for PrEP

The following criteria will be used to offer PrEP:

- HIV-negative by routine rapid antibody test
- Absence of symptoms of acute HIV infection (see Table 1)
- Willing and able to take PrEP as prescribed
- No contraindications to TDF or FTC
- Adolescents >35kg in weight; if <15 years in age, adolescents should be Tanner stage 3 (sexual maturity rating) or greater.

4.3. Contraindications for PrEP

The following are contraindications for PrEP use:

- HIV infection
- Creatinine clearance of less than 60mL/min

Table 1. Acute Viral Symptoms of HIV Seroconversion [6, 7]

Symptom	Sign
Malaise, anorexia, myalgia, headache, sore throat, sore glands, rash	Fever, sweating, viral meningitis, generalised lymphadenopathy, hepatosplenomegaly, pharyngitis, truncal rash, orogenital herpetiform ulceration, oral/oesophageal candidiasis, cervical adenopathy

If the client has symptoms or signs of acute HIV infection, PrEP should be postponed until symptoms subside and a repeat rapid HIV test after 4 weeks remains negative.

4.4. Baseline Investigations

After documenting eligibility for PrEP use, several baseline investigations should be conducted before the individual can be initiated on PrEP (refer to Table 2). HIV testing should be performed on the same day that PrEP is initiated. Specimens collected for other laboratory tests (including creatinine and hepatitis B surface antigen) should be sent to the laboratory and the PrEP user can be contacted if the test results require additional action, confirmation.

Table 2. Baseline Investigations

Investigation	Action to be taken
HIV test (use algorithm in National HTS guidelines)	To assess HIV infection status. If client is HIV-positive, initiate on ART If client is HIV-negative, screen for PrEP
Estimated glomerular filtration rate (eGFR)	If eGFR is less than 60 ml/min, DO NOT initiate PrEP. Repeat in 2 weeks and if eGFR is above 60 ml/min, start PrEP.
Hepatitis B surface antigen (HBsAg)	If HBsAg-: start PrEP and vaccinate, if available If HBsAg+: start PrEP, and refer to a doctor for liver function monitoring and management of Hepatitis B infection.
Syndromic STI screening	To diagnose and treat STI (syndromic or diagnostic STI testing).
Pregnancy screening	As per WHO guidance, the use of PrEP is not contraindicated in pregnancy. [9,10,11] If the client is not pregnant, offer contraception.
Clients with acute or chronic hepatitis B infection can be safely initiated on PrEP but require liver function monitoring. [8]	

4.5. PrEP in Pregnant and Breastfeeding Women

As per WHO recommendations, pregnant and breastfeeding women at substantial risk of HIV infection may be considered for PrEP.[9,10,11] The scenarios outlined below, provide guidance on the provision of PrEP among pregnant and breastfeeding women:

1. PrEP should be considered for HIV negative women already taking PrEP, who become pregnant and remain at substantial risk of HIV (the choice of whether to continue or discontinue should be made by the woman following a discussion with the clinician on the risks and benefits of PrEP).

2. PrEP should be considered for HIV negative breastfeeding women who are at substantial risk of HIV or in serodiscordant relationships where there is no evidence of viral load suppression in the HIV positive partner.

3. Pregnant women not on PrEP, considered to be at substantial risk of HIV may be referred to a medical practitioner to discuss the potential risks and benefits of initiating PrEP during pregnancy.

Eligible women must be offered PrEP together with acute HIV infection screening, adherence counselling, safety monitoring and three-monthly HIV testing.

4.6. PrEP and Hepatitis B

TDF and FTC both have hepatitis B antiviral activity. Discontinuation of PrEP may cause serious liver damage resulting from reactivation of HBV. PrEP users with chronic hepatitis B should be carefully monitored when they discontinue PrEP. Some PrEP users may opt to continue using tenofovir to control their hepatitis, even if they no longer require these drugs for the indication of PrEP.

4.7. Prescription of PrEP drugs

The recommended regimen is TDF/FTC 1 tablet by mouth (PO) daily. The drugs can be taken anytime of the day, with or without food, and can be stored at room temperature.

Prescription intervals:

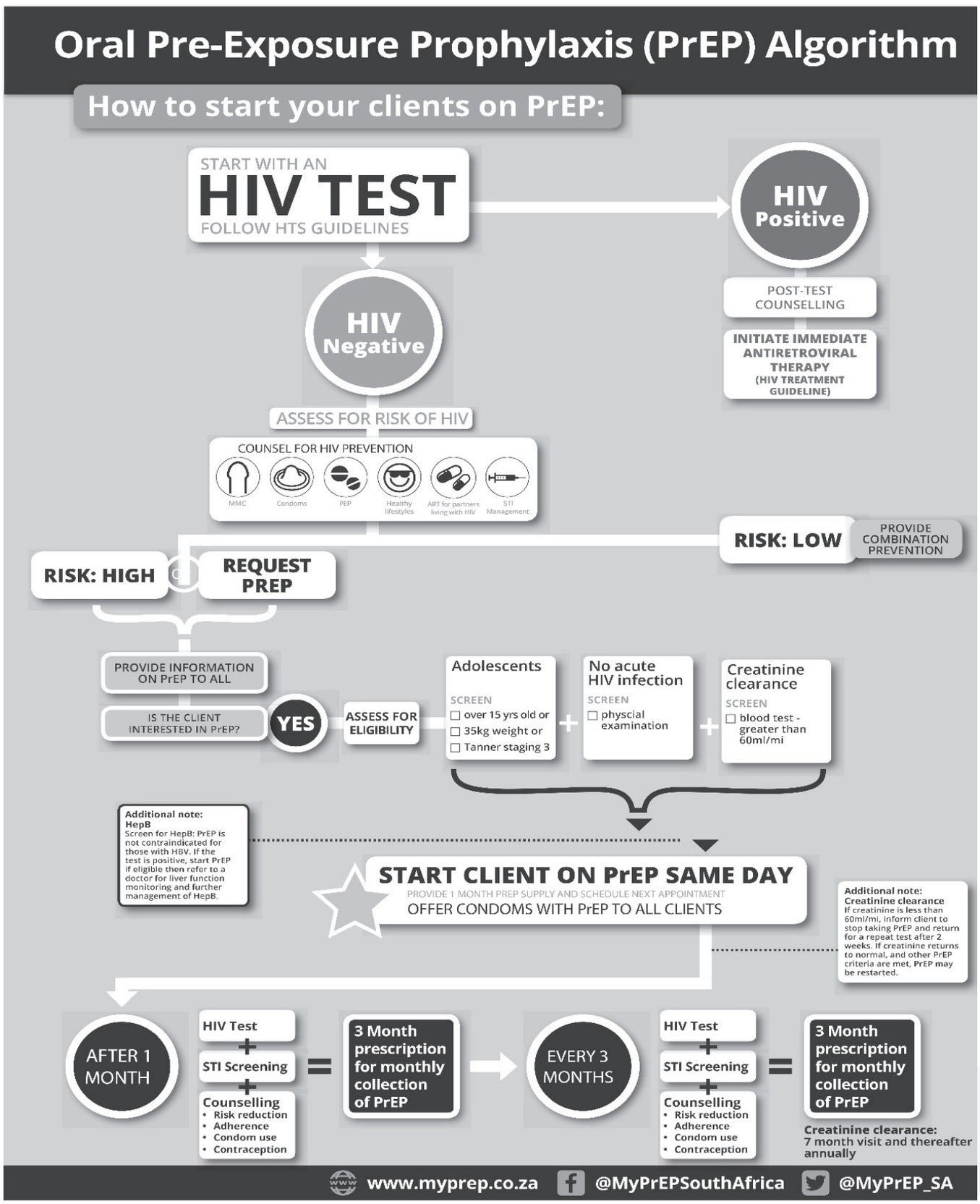
- At initiation – provide 1- month supply
- At 1 month visit – repeat HIV test and provide 3-month prescription (for collection every month)
- Every 3 months – repeat HIV test and provide 3-month prescription (for collection every month)

IMPORTANT

Clients initiating PrEP need 7 days of daily dosing to reach adequate tissue levels of PrEP drugs. During this period, other protective precautions should be used, such as abstinence or condoms.

Check for last potential HIV exposure in individuals wanting to stop taking PrEP. PrEP should be continued for 28 days after the last potential HIV exposure in those wanting to cycle off PrEP.

Figure 1. PrEP Screening and Art Initiation Algorithm



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4.8. PrEP Counselling

Client education is critical to the success of PrEP as part of a comprehensive HIV prevention plan. Providers should educate and counsel PrEP users about PrEP (refer to Table 3) and should provide them with other appropriate prevention options such as male and female condoms.

Risk-reduction counselling is a behavioural intervention that attempts to decrease an individual's likelihood of acquiring HIV and other STIs, and should be implemented as part of HIV prevention counselling, with sexual reproductive health and contraceptive counselling at all follow-up visits for PrEP users.

The main objective of risk-reduction counselling is for clients to learn how to assess individual HIV risk and set realistic goals for behaviour change that may reduce their risk of contracting HIV and other STIs, as well as reduce unwanted pregnancies.

Table 3. Key counselling messages before PrEP initiation and during follow-up visits.

Topic	Key Messages
What is PrEP?	PrEP is ARV medication that can be taken by HIV-negative persons before exposure to HIV to prevent an HIV infection. PrEP is an additional HIV prevention option and, where possible, should be used in combination with other interventions such as condoms. PrEP does not protect against other STIs or prevent pregnancy.
PrEP is not for life	PrEP is taken for as long as the individual is at risk for HIV infection. PrEP can be discontinued if the individual is no longer at risk.
PrEP works if taken	For PrEP to be effective, it must be taken every day. Consistent use requires that PrEP be included in the daily routine. If a dosage is missed, the client must take the PrEP drug as soon as he or she remembers and continue to take daily as before. It can be taken with or without food and at any time of the day.
Side effects	PrEP is safe, with no side effects in most of the users. Some individuals may report minor side effects in the first month of PrEP use, such as diarrhea, headache, abdominal pain and nausea. Major side effects associated with PrEP are very rare. *
Drug interactions	Taking alcohol will not reduce the effectiveness of PrEP. PrEP can be taken with any kind of contraception and sex hormones.
Starting and stopping PrEP	7 consecutive days of PrEP are needed before achieving full protection from HIV infection. PrEP should be continued for 28 days after the last potential HIV exposure in those wanting to cycle off PrEP. The client should notify the provider if he or she decides to stop taking PrEP.
Pregnancy and breastfeeding	WHO recommends that PrEP is safe for use in pregnant or breastfeeding women at substantial risk of HIV infection. [9,10,11]
Safer conception	In serodiscordant relationships, PrEP can be safely used by the HIV negative partner for safe conception.
Visit schedule	The client must return for a month one and thereafter 3-monthly for follow-up HIV testing, counselling and safety monitoring visits.
*Major side effects are extremely rare and may include renal toxicity and metabolic complications decreased bone mineral density (which is reversible), extremely small risk of lactic acidosis and hepatic steatosis or steatohepatitis.	

4.9. PrEP clients who test HIV-Positive

4.9.1. HIV-Positive prior to initiation of PrEP

Clients who test HIV-positive must be initiated on ART or referred for ART as soon as possible, regardless of CD4 count. They must be linked to HIV care, treatment, and support. Where possible, their partners should be encouraged to test for HIV.

4.9.2. HIV-Positive after initiation of PrEP

HIV seroconversion after initiating PrEP can occur and may be due to:

- **People who take PrEP drugs inconsistently** or do not take it as prescribed. PrEP drugs must be taken daily for it to be effective.
- **People who stop PrEP for a variety of reasons.** It is important to quantify this group and assess the reasons for their disengagement in care to inform programme improvement.
- **PrEP failure:** People who take PrEP consistently as prescribed and become

The provider must engage the client and assess which of the factors stated above may have led to seroconversion and this must be documented in the PrEP clinical form. As soon as an HIV-positive test has been confirmed, the individual must be initiated ART or referred for ART initiation, regardless of CD4 count. They must be linked to HIV care, treatment, and support. Where possible, their sexual partners should be encouraged to test for HIV.

4.10. PrEP Follow-Up and Monitoring

Table 4. PrEP Follow-Up and Monitoring

Activity	Following oral PrEP initiation
Confirmation of HIV-negative status	At initiation, at 1 month, then every 3 months
Address side effects	Every visit
Adherence counselling	Every visit
Creatinine clearance test	At initiation, at 7 months, then annually
STI screening and treatment	Every visit
PrEP medication issuance	1-month supply, then 3 monthly prescription for monthly collection
Behavioural sexual risk reduction counselling	Every visit

4.11. Discontinuation of 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 benefits

PrEP medication should be continued for 28 days after the last potential HIV exposure to ensure protection.

4.12. Monitoring of the PrEP Programme

Routine monitoring of the PrEP programme is essential to assess uptake, effective use, and safety. The data collected will also assist with forecasting demand to ensure sufficient and an uninterrupted supply of all the required commodities.

To facilitate standardised and systematic monitoring of the programme, all PrEP service points must use the PrEP Clinical Form to collect client data. A copy of the clinical form can be found in Appendix 1. PrEP providers must ensure that the form is completed in detail and kept in the client file at the healthcare facility. The information contained in the clinical form must then be transferred into TIER.Net.

The following indicators will be used for the routine monitoring of the PrEP Programme to assess uptake, safety and continued use.

Table 5. PrEP Indicators

Indicator	Definition	Source document	Point of collection
PrEP Uptake	Number people who received PrEP for the first time in the reporting period.	PrEP Clinical form	At PrEP initiation
Continuation on PrEP	Number of individuals, inclusive of those newly enrolled, that received PrEP during the reporting period.	PrEP Clinical form	At monthly follow-up visit

APPENDIX 1: PrEP Counselling Guide

Oral Pre-Exposure Prophylaxis (PrEP)
Counselling Guide

1. Pre-test information
2. HIV test
3. Post-test counselling

For clients who are HIV-negative

4. Assess your client's risk of getting HIV.

Discuss your client's risk, explore the following:

Be sensitive and non-judgmental!

- ☐ Do you ever have unprotected sex (not using a condom)?
- ☐ Do you have unprotected sex with a partner/s who are HIV-positive?
- ☐ Do you ever have unprotected sex with a person whose HIV status you don't know?
- ☐ Do you ever have sex under the influence of alcohol and/or drugs?

Individuals who answer YES to any of these questions or ask for PrEP should be considered for PrEP.

5. Inform your client that PrEP, a pill that prevents HIV, is available at this clinic.

6. Find out if your client is interested in knowing more about PrEP.

7. Provide information about PrEP - if your client is interested and wants to know more.

- PrEP is an ARV pill used to **PREVENT** HIV infection.
- PrEP is for HIV-negative people.
- PrEP is taken daily.
- PrEP is safe to take!
- PrEP does not protect you from getting other STIs.
- PrEP does not prevent you from getting pregnant.
- PrEP can be stopped at any time that you do not need it.

Always try to use a condom as well as PrEP.

Key messages

PrEP works best when you take it every day!

Because PrEP does not protect you from STIs or getting pregnant, it is best to use with condoms and contraception, where appropriate.

8. If client is interested in PrEP tell him/her that the nurse will check the following:

Adolescents
- over 15 yrs old or
- weigh more than 35kg

No signs of HIV infection
- physical examination
- HIV test

Kidneys are functioning well
- blood test

If all of these tests are OK, the client could start PrEP immediately.

You do not have to wait for the blood results to start PrEP.

9. Starting PrEP

Provide the correct information and education regarding PrEP:

- You will have to take PrEP pills for **7 days,** every day, before you are fully protected from an HIV infection.
- Use a condom in these first 7 days.
- You will get the best protection if you take PrEP pills every day.
- You can stop taking PrEP if you are no longer at risk.
- If you want to stop PrEP, continue to take PrEP pills for 28 days before stopping.

Clinic visits:

Pill-taking

- Remember to take PrEP every day.
- PrEP tablets can be taken any time of day, with food or without food.
- If you forget to take a tablet, take it as soon as you remember.
- Set an alarm or link pill taking to something else that you do every day – like having your morning tea or brushing your teeth before you go to bed.
- PrEP is safe even if you are taking hormonal contraceptives, sex hormones or non-prescription drugs.
- PrEP is safe with alcohol.

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APPENDIX 2: PrEP Clinical Form

PrEP Clinical form (Initiation)

First name		Folder #	
Surname		Phone #	
DOB	dd / mm / yy **Gender:** M / F / TG	Address	
ID Number			

Instructions: Please use the below form to capture initiation, continuation, discontinuation, and re-initiation for PrEP. If a patient discontinues, continue the record with the corresponding date of discontinuation. Should a patient re-start PrEP, re-initiation and subsequent visits will be captured into this same form. Adherence support and other notes can be captured further below.

Steps Prior to PrEP Initiation/Re-Initiation

Date of Visit	HIV Test Result	PrEP Counselling Conducted?	Proceed with Screening?	PrEP Screening					
				Creatinine (eGFR)	Pregnancy	Weight (Kgs)	Hep B Result	STI Screening	Decide to Initiate?
/ /	+ / -	Y / N	Y / N		+ / - / NA			+ / -	Y / N
/ /	+ / -	Y / N	Y / N		+ / - / NA			+ / -	Y / N
/ /	+ / -	Y / N	Y / N		+ / - / NA			+ / -	Y / N
/ /	+ / -	Y / N	Y / N		+ / - / NA			+ / -	Y / N

PrEP - Initiation/Re-Initiation and Monitoring

Original PrEP Initiation Date	/ /	Transfer In:	Date: / /	From Clinic:

# of months on PrEP	Next visit Date:	Actual visit:	Staying on PrEP?	Test Results (if applicable)						
				HIV Test	Creatinine (eGFR)	Weight (Kgs)	Pregnancy	STI Screen	**Outcome** (RIP, LTF, TFO, Sero, DNA, Disc)	Month of Outcome
0	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
1	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
2	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
3	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
4	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
5	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
6	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
7	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
8	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
9	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
10	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
11	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
12	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
13	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /
14	/ /	/ /	Y / N	+ / -			+ / - / NA	+ / -		/ /

Notes: Reason for discontinuation / adherence support / allergies / medical history / hospitalisations / TB history. *Please state reason for discontinuation in detail (client's choice / change in risk profile / adverse effects, etc.)

NB: Please affix any copies of additional notes or laboratory results that are necessary.

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