TITLE: ORAL PRE-EXPOSURE PROPHYLAXIS

INTRODUCTION

Zimbabwe remains one of the countries burdened by the HIV epidemic. 1,3 million people are living with HIV (prevalence~14.9%) and the number of new HIV infections remains high (incidence~ 0.48%). Oral Pre-exposure prophylaxis is now included as additional option for people at substantial risk of HIV infection in the context of combination HIV prevention package in Zimbabwe. This training package will provide information on PrEP so that service providers will be able to know why PrEP is given, which clients should receive it, how to prescribe it, and how to manage clients on it. As the use of PrEP is an evolving area, it is expected that these documents will require updating over time as new information regarding PrEP arises and implementation experiences accumulate.

TRAINING OBJECTIVES

Broad objective

The objective of this module is to provide health workers with information on pre-exposure prophylaxis (PrEP) so that can they can be able to know why PrEP is given, to which clients, prescribe it and manage clients on PrEP.

Specific objectives

By the end of this module, participants will be able to:

- Identify eligible candidates for PrEP.
- Conduct an individualized risk assessment.
- Educate and counsel PrEP candidates and users.
- Conduct clinical and laboratory assessments during the initial PrEP visit.
- Prescribe PrEP.
- Conduct clinical and laboratory assessments during follow-up PrEP visits.
- Use PrEP monitoring and evaluation (M&E) tools effectively.

STRUCTURE OF THE TRAINING

1. PrEP Basics
2. PrEP Screening and Eligibility
3. Initial and Follow up PrEP Visits
4. Monitoring and managing PrEP Side Effects, Seroconversions and Stigma
5. Special Considerations for AGYW
6. Monitoring and Evaluation for PrEP

MODULE 1: PREP BASICS

By the end of this session, participants will be able to:

- Define what PrEP is and differentiate PrEP from PEP and ART.
- Conceptualize PrEP as part of combination HIV prevention
- Understand the evidence for PrEP and why it is given.
- Address the concerns surrounding PrEP implementation

BACKGROUND

Different people have different HIV prevention needs. For a given individual, prevention needs can change over time. No single prevention intervention can fully address all prevention needs. To prevent HIV infection, a combination of structural, behavioral, and biomedical interventions are used. The combination of HIV prevention approaches used are based on both epidemiological and demographic evidence of what is needed in a particular setting. Combining approaches result in synergies with greater impact than single interventions alone

Antiretroviral drugs (ARVs) are now used as additional tools in combination prevention. The use of ARVs for HIV prevention is well established; we have been using ARVs to prevent mother-to-child transmission of HIV (PMTCT) for post-exposure prophylaxis (PEP) for many years.

The combination of HIV prevention approaches used are based on both epidemiological and demographic evidence of what is needed in a particular setting. Combining approaches result in synergies with greater impact than single interventions alone

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COMBINATION HIV PREVENTION

Combination prevention refers to a systematic approach to implementing a range of HIV prevention interventions: behavioural and biomedical in synergy with structural interventions. This means that the different interventions are delivered in combination and tailored to the needs of the different individuals and population groups at risk of HIV infection. The combination approach recognizes that an individual's risk of HIV infection and their HIV prevention needs change over time

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Structural interventions aim to address social, economic, political, environmental, cultural, and also organizational, community, legal, or policy factors that influence vulnerability and predispose different groups of people to HIV infection.

Behavioural interventions support behaviour change to reduce the risk of HIV infection.

Biomedical interventions are particular tools, commodities, or mechanisms that lower infectiousness of HIV infected persons and/or susceptibility of HIV-negative persons to HIV. Within biomedical interventions is the use of antiretroviral drugs for HIV prevention.

It is critical to include all the combination strategies in reducing te risk of HIV acquisition by HIV negative people

Structural	Behavioral	Biomedical
• Policies • Laws • Regulatory environment • Cash transfer	• Education • Counselling • Stigma reduction • Harm reduction • Adherence interventions	• HTS • Condoms • VMMC • PMTCT • STI treatment • ART • PrEP • PEP

DISCUSSION

What are the policies, laws and regulatory issues that are facilitators and barriers to HIV prevention?

What are the challenges with the different components of the combination HIV prevention package?

DEFINING PRE-EXPOSURE PROPHYLAXIS

PrEP is the use of antiretroviral 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

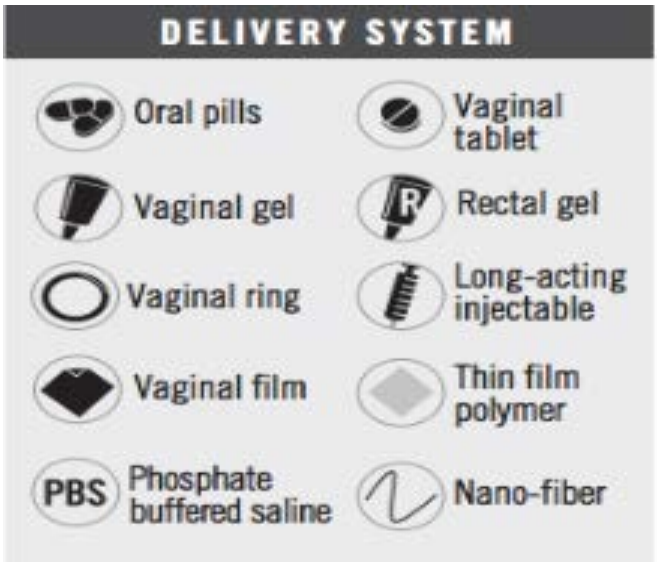
The WHO recommends that oral PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention.

Substantial risk of HIV infection is defined as an incidence of HIV infection between 3 per 100 person-years in the absence of oral PrEP. Identifying and offering oral PrEP to those at substantial risk leads to great individual benefit, strong epidemiological impact, and optimal investment in resources.

KEY QUESTION

Who is at substantial risk of HIV infection?

Forms of PrEP under trial!!



Indicators of substantial risk of HIV infection vary depending on local HIV epidemiology and population group

Inconsistent use of condoms (male or female), including an intention to use condoms during sex with some occasional omissions or accidents, increases HIV risk. Social desirability bias in reporting condom use may occur, so PrEP could be considered for people reporting any intercourse without a condom or concerns about their future use of condoms. For example, someone who reports a desire to stop using condoms may be already having sex without condoms.

Recently diagnosed STIs are often indicators of risk of sexual acquisition of HIV. The predictive value of STI indicators varies by region, the type of STI and a person's demographic characteristics. A new diagnosis of syphilis or genital herpes is a strong predictor of HIV risk among men who have sex with men in most settings and among heterosexual men and women in areas of high HIV prevalence. PrEP services should be prioritized; local epidemiology will be essential to guide decisions about when to offer PrEP and to which populations.

Requesting PrEP has been shown to be an indicator of substantial risk. HIV incidence among people requesting PrEP has been higher than expected from observational studies in the same locality. People at high risk of acquiring HIV infection who request PrEP tend to have greater PrEP uptake, adherence and retention. Clinicians should consider any request for PrEP seriously, especially for individuals in settings where the local epidemiology indicates likely substantial HIV risk in their population group.

People who use and/or inject drugs are often at substantial HIV risk. WHO recommends a package of effective HIV services be provided for all people who inject drugs, including harm reduction (in particular opioid substitution therapy and needle syringe programmes). When these interventions are available, the risk of HIV transmission is significantly reduced. Providing these services should be a priority.

GROUP EXERCISE

What are some similarities and differences between Pre-Exposure Prophylaxis (PrEP) and Post-Exposure Prophylaxis (PEP)?

Are both PEP and PrEP used in children, adolescents, pregnant women?

PEP (post-exposure prophylaxis) means taking antiretroviral medicines (ART) after being potentially exposed to HIV to prevent becoming infected. PEP should be used only in emergency situations and must be started within 72 hours after a recent possible exposure to HIV

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

PEP regimens for adults

- Tenofovir 300 mg orally once daily

plus

- Lamivudine 300 mg orally once daily

Plus

- Atazanavir (300mg)/ ritonavir 100mg orally once daily

The above regimen is given for one month.

PrEP regimens for children

AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children 10 years and younger.

ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens.

LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years.

An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.

DISCUSSION

What are some similarities and differences between 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 they:

- acquire HIV infection.
- are no longer at substantial risk for HIV infection.
- decide to use other effective prevention methods.

ART is taken by HIV infected persons for treatment.

PrEP is used by HIV uninfected persons for prevention. There are alternative prevention methods a person can use.

HIV treatment requires life-long therapy with constant dosing.

PrEP is needed during periods of high HIV risk. Clients can discontinue PrEP if they feel they are no longer at risk (e.g. in a mutually monogamous relationship with HIV-negative partner).

Or if they decide to use other effective prevention methods (e.g. consistent use of male or female condoms).

Motivation for adherence is different: ART is taken by HIV infected persons so they can remain healthy, while PrEP is taken by HIV uninfected persons to prevent infection.

HIV treatment regimens

- Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg + Efavirenz (EFV) 400mg
- Tenofovir (TDF) 300mg+Lamivudine (3TC) 300mg+Efavirenz(EFV) 600mg
- Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg + Nevirapine (NVP) 200mg

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WHY WE NEED PREP

There are several effective HIV prevention interventions already (e.g. condoms, harm reduction for PWID), we need another prevention intervention because…

- New HIV infections still occur despite prevention efforts
- New HIV infections among priority and key populations are quite high

Despite other HIV prevention strategies to prevent HIV infection, new infections still occur. And high among priority and key populations. PrEP provides an additional prevention intervention to be used with existing interventions (such as condoms). It is not meant to replace or be a substitute for existing interventions.

EVIDENCE FOR PREP

There is evidence of efficacy from several clinical trials among MSM, heterosexual men and women, and people who inject drugs. For study participants with Truvada in plasma, efficacy reached 92%.

There were disappointing results in the FEMPreP and VOICE trials which were discontinued for futility.

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 Kingdon)	545 MSM and transgender women	Randomized to daily oral TDF-FTC immediately or delayed	Immediate TDF-FTC: 86% ↓

References for some studies

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

Partners PrEP - Baeten JM, et al.N. Engl J M.2012 :367 :399-410

TDF 2 - Thigpen MC, et al. N Engl J Med.2012 ; 367 :423-434

FEM PrEP -Van Damme L, et al. N Engl J Med.2012 :357 :411-422

Bangkok TDF study- Choopanya K, et al. Lancet.2013 ;381 :2083-2090

Oral PrEP taken daily during periods of substantial risk of HIV infection, is a highly-effective prevention strategy, and can reduce the risk of acquisition of HIV through sexual intercourse by more than 90%. The level of protection provided by oral PrEP does not differ by age, sex, or mode of acquiring HIV - rectal, penile or vaginal exposure; however, the level of protection is strongly correlated with adherence. High adherence to oral PrEP results in a high level of protection from HIV infection whereas suboptimal adherence does not offer the expected protective benefits.

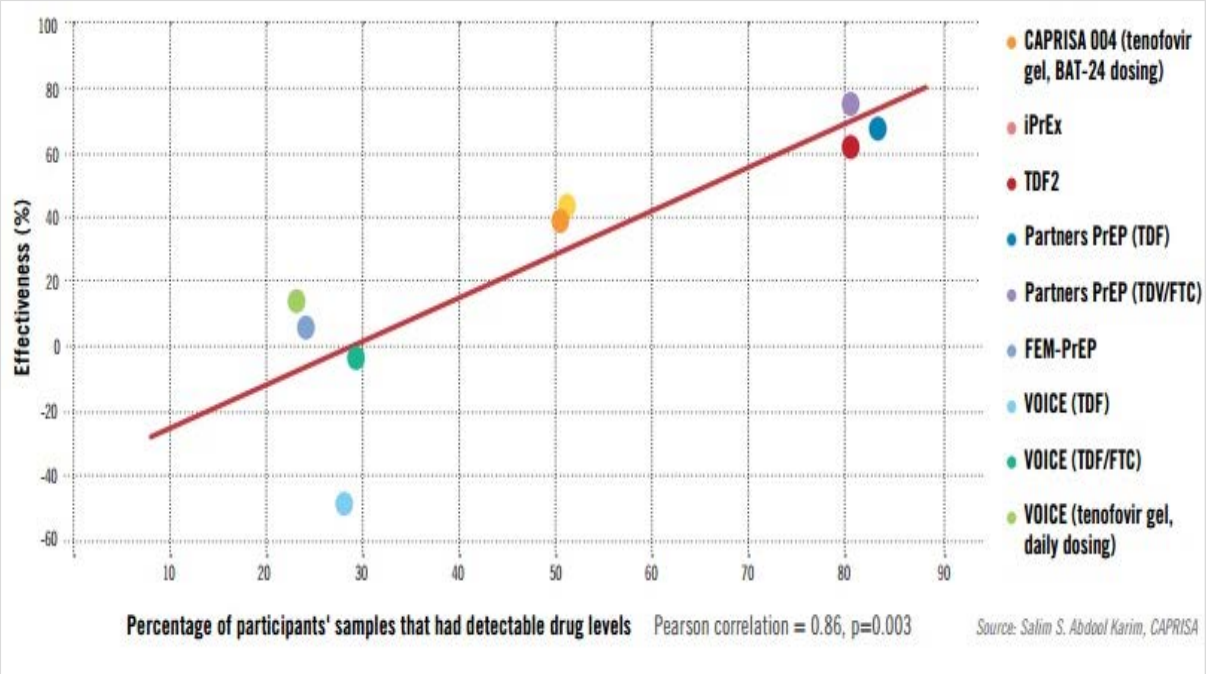

Figure 5Effectiveness and adherence in trials of oral and topical Tenofovir based prevention

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FREQUENTLY ASKED QUESTIONS AND ANSWERS

Is PrEP safe?

PrEP showed no evidence of increased proportion of adverse events. Analysis of results of many PrEP studies show that 90% of participants had no side-effects!

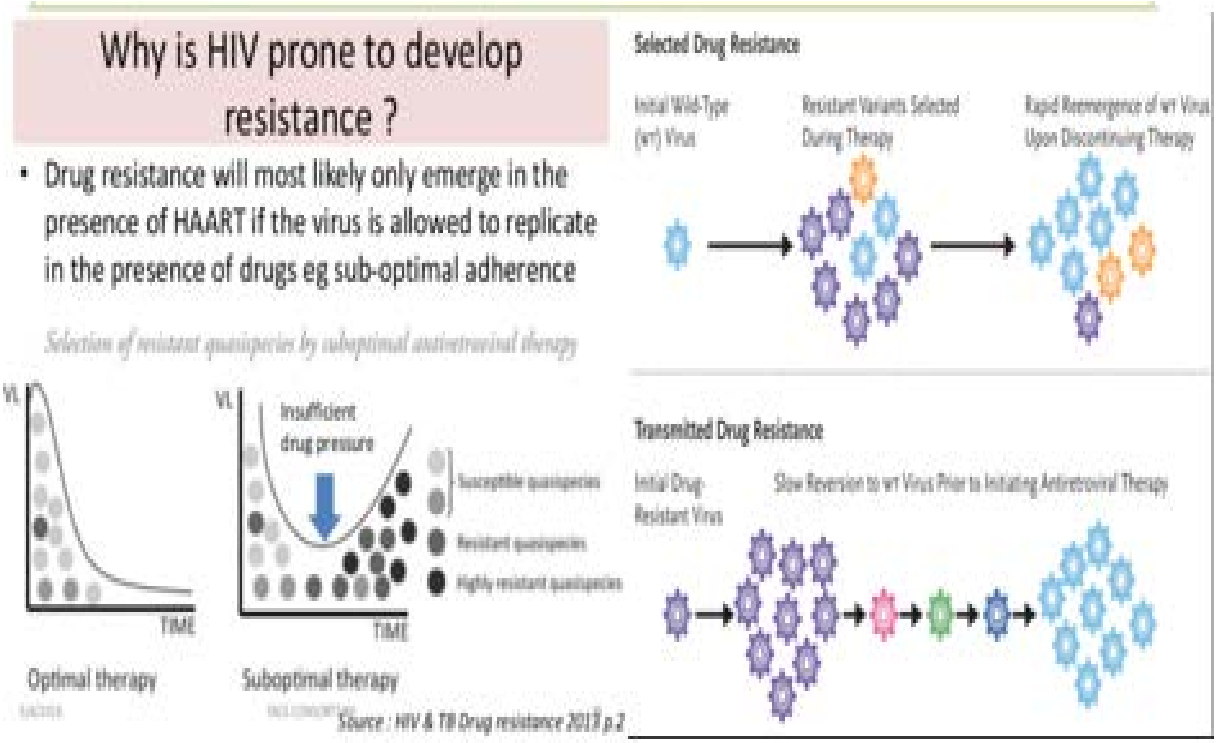
PrEP is safe!

Approx. 10% in clinical trials experienced mild, short-term side-effects like nausea, tiredness, gastrointestinal symptoms (flatulence) and headache.

Will PrEP users engage in riskier behaviours? 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 behaviour 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, gonorrhoea, chlamydia, or HPV

PrEP should be provided within a package of prevention services, including STI screening and management, risk reduction counselling, condoms, contraceptives, etc.

MODULE 2: SCREENING FOR PREP AND INITIATION

Module objectives

By the end of this session, participants will be able to:

- Recognize the indications for PrEP
- Identify people at risk and at substantial risk for HIV infection; including priority and key populations
- Conduct HIV risk assessment for PrEP
- Know when and how to prescribe PrEP

WHO recommendation for PrEP

> 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]

Oral PrEP is an additional prevention choice in addition to the standard combination prevention approaches. PrEP is a choice that ultimately the client should have when accessing health services. Offer as an additional prevention choice

Deliver PrEP with comprehensive support

- Adherence counselling
- Legal and social support
- Mental health and emotional support
- Contraception and reproductive health services

Who should be offered PrEP?

PrEP will be offered to all individuals at substantial risk of HIV infection. The policy on who should be offered PrEP is broad to ensure equitable access and to avoid stigmatizing individuals, groups or the product – even if initial implementation prioritizes high-risk groups

In Zimbabwe, groups that are likely to be at substantial risk of HIV infection include:

- Female and male sex workers;
- Sero-discordant couples (HIV negative partner)
- Adolescent girls and young women;
- Pregnant women in relationships with men of unknown status
- High-risk men (MSMs, prisoners, long distance truck drivers) and
- Transgender people

Indications for PrEP

Indications for PrEP by history over the past 6 months:

- HIV negative and sexual partner with HIV who has not been on effective therapy for the preceding 6 months OR
- HIV negative and sexually active in high HIV prevalence settings AND any of the following….

AND any of the following:

- Vaginal or anal intercourse without condoms with more than one partner, OR
- A sexual partner with one or more HIV risk factors, OR
- A history of an STI by laboratory testing or self-report or syndromic STI treatment, OR
- Any recurrent use of PEP, OR
- Requesting PrEP

Contraindications for PrEP

Contraindications must be ruled out before starting PrEP, these include:

- HIV positive status
- Unknown HIV status
- Allergy to any medicine in the PrEP regimen
- Unwilling/unable to adhere to daily PrEP
- Known renal impairment
- Estimated creatinine clearance <60 cc/min

What is required before PrEP Initiation?

Conduct a rapid HIV test to rule out existing HIV infection preferably on the same day that PrEP is being started.

Take a complete medical history and full physical examination to rule out any signs or symptoms of an acute viral syndrome, including a flu-like illness, then consider the possibility that acute HIV infection could be the cause. In such circumstances testing for HIV RNA or antigen is recommended or retest using rapid HIV test 4 weeks later

Measure blood creatinine before starting PrEP and at every 6 months after PrEP where available. Blood creatinine is mandatory in people with comorbid conditions that can affect renal function, such as diabetes mellitus and uncontrolled hypertension

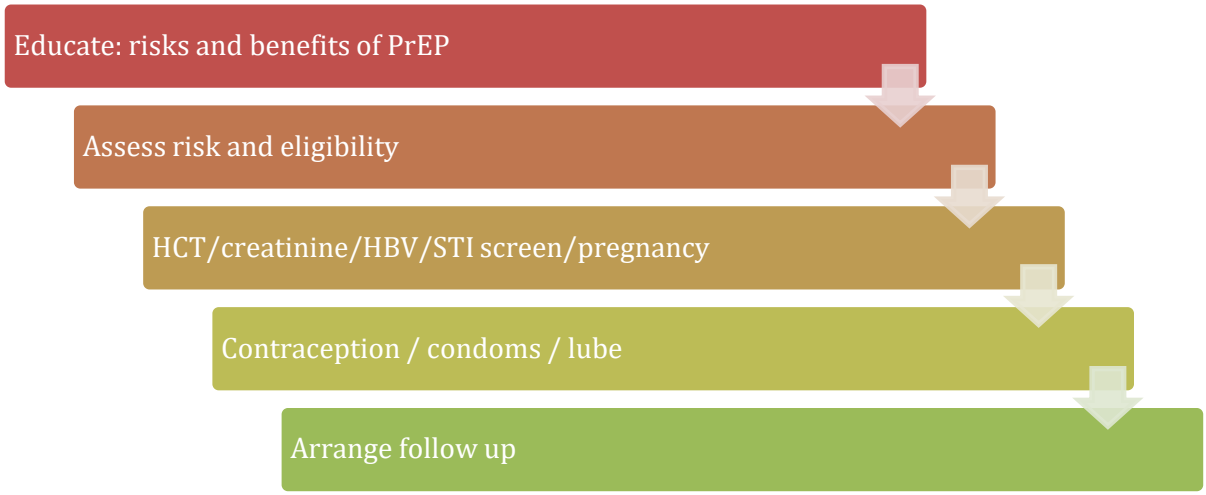
In addition, conduct:

- HIV risk assessment using a screening tool
- Adherence counselling

What is recommended before PrEP initiation?

- Hepatitis B test
- Blood Creatinine level check
- Pregnancy test
- STI Screening and Treatment

First visit



HIV risk assessment

Review the current risk assessment/ screening tool

Screening Form for PrEP
Start Up or Follow-Up Visits

Date of Birth (DD/MM/YYYY) _____/_____/_____

What is your sex? Male [ ] Female [ ]

Tick what is applicable.

* ***Consider offering PrEP***

1. In the past 6 months: How many people did you have vaginal or anal sex with?

	0	1	2+*
Men			
Women			

2. In the past 6 months: Did you use a condom every time you had sex?

Yes	No*	Don't Know*

3. In the past 6 months: Did you have a sexually transmitted infection?

Yes*	No	Don't Know*

4. Do you have a sexual partner who has HIV? Yes* [ ] No [ ] Don't Know* [ ]

	Yes	No*	Don't Know*
a. If, "Yes, has he or she been on therapy for 6 or more months?			
b. If "Yes," has the therapy suppressed viral load?			

** ***Consider offering PEP***

5. In the past 3 days: Have you had sex without a condom with someone with HIV who is not on treatment?

Yes**	No	Don't Know

*** ***Consider acute HIV***

6. Have you had a "cold" or "flu" such as sore throat fevers, sweats, swollen glands, mouth ulcers, headache, or rash?

Yes***	No	Don't Know

ROLE PLAY

Practice in pairs using different scenarios: AGYW, Sex worker, MSM, sero-discordant

What are the potential challenges with some of these questions?

Are there other questions that should be asked to assess risk?

DISCUSSION

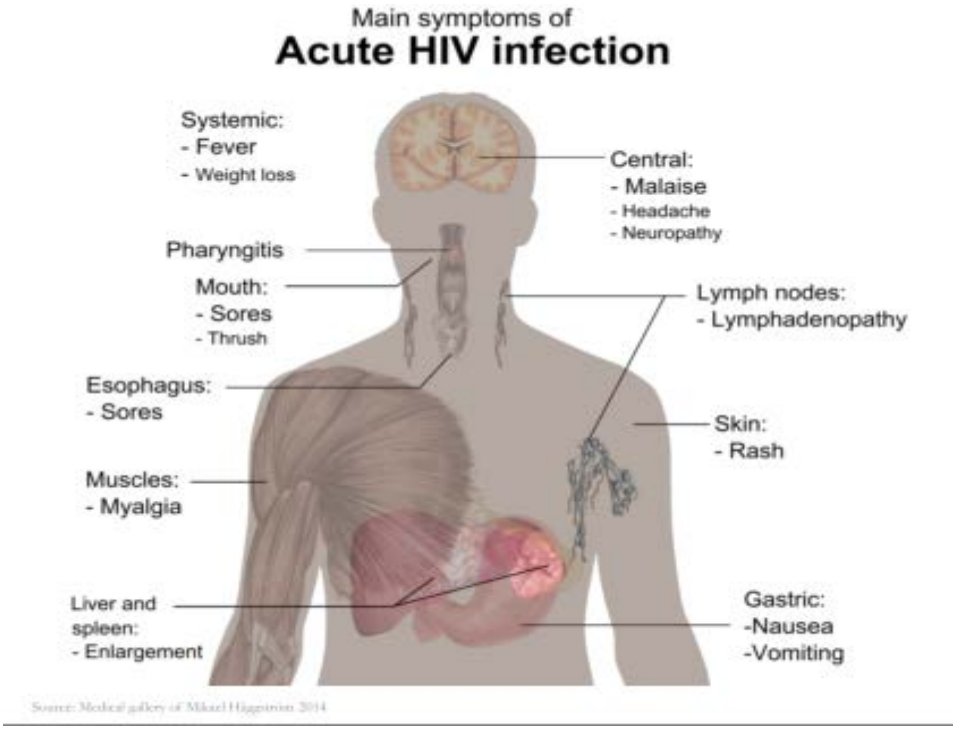
Review PrEP Practical screening questions (Annexe 1)

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 below depicts some of the presenting signs and symptoms of AHI.

DO NOT START PREP IN CLIENTS WITH SUSPECTED AHI!!



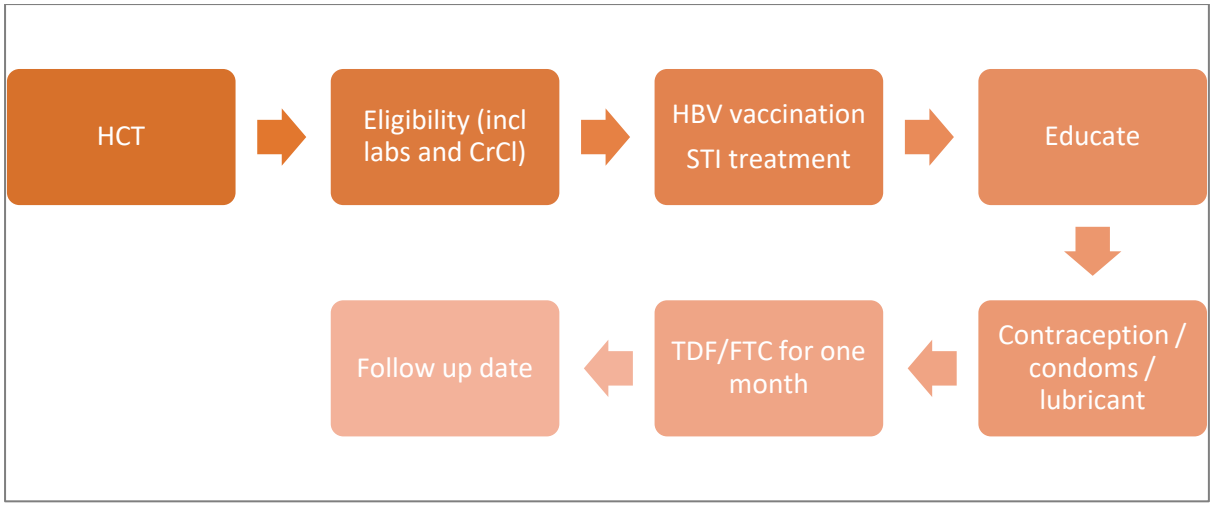
Diagnosis of acute HIV infection

During AHI, antibodies might be absent or be below 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.

PrEP INITIATION AND REGIMENS

PrEP should be administered by medical doctors and nurses trained in ARV management.



	Drug	Dosage	Duration
Preferred Regimen	Tenofovir (TDF (300mg) plus Emtricitabine (FTC) (200mg)	Fixed dose combination one tablet once a day	Period of substantial risk
Alternative Regimens	TDF (300mg) plus 3TC (300mg)	Fixed dose combination one tablet once a day	Period of substantive risk

Key points: duration of protection

- Daily dosing in the period of substantial risk
- PrEP reaches maximum effectiveness after 7 doses.
- Full protection may require 4 daily doses for anal sex
- Full protection may occur after 7 daily doses for vaginal sex
- Unlike a patient on lifelong ART, a PrEP client may be discontinued from PrEP when they are no longer at substantial risk of HIV infection
- PrEP medications should be continued for 28 days after the last potential HIV exposure in those wanting to cycle off PrEP

When to stop PrEP

The duration of PrEP use may vary and individuals are likely to start and stop PrEP depending on their risk assessment at different periods in their lives. PrEP can be

stopped 28 days after the last possible exposure to HIV if the client is no longer at substantial risk for HIV infection. It can also be stopped if client:

• Has a positive HIV test

• Develops renal disease (Creatinine Clearance <60ml/Min)

• Has an adverse medicine reaction and

• In sero-discordant couples, when HIV infected partner on ART has achieved viral suppression

Objectives

MODULE 3: CLIENT MONITORING, FOLLOW UP AND ADHERENCE

By the end of this session, participants will be able to:

- How to follow up and monitor clients on PrEP
- Conduct adherence counselling
- Explain the relationship between PrEP effectiveness and adherence
- Know management of PrEP side effects
- Understand when to stop PrEP
- Clinical and laboratory monitoring

- Management of adverse events

PREP CLIENT FOLLOW UP SCHEDULE

Clients on PrEP require regular visits with the health provider. After initiating PrEP the client should be reviewed after 1 month to:

- monitor adherence
- Assess for side effects
- resupply of medicines

Thereafter 3 monthly visits are conducted to monitor client and resupply medicines. Some interventions are mandatory while others are recommended but should not hinder PrEP if not available

Required for follow up

Intervention	Schedule following PrEP initiation
Confirmation of HIV negative status	**Every 3 months**
Address medicine side effects	**Every visit**
Provide STI screening, condoms, contraception or safer conception services	**As needed**
Counselling regarding: o **effective PrEP use (adherence)** o **prevention of STIs,** o **issues related to mental health,** o **intimate partner violence,** o **substance use**	**Every visit**

Recognition of symptoms of sexually transmitted infections and management	**Every visit**
HIV risk assessment	**Every visit**

Recommended for follow up (should not hinder ongoing access)

Intervention	Schedule following PrEP initiation
Estimated creatinine clearance.	Every 6 months. • Consider more frequently if there is a history of conditions affecting kidneys (creatinine clearance <60ml/min) • consider less frequently if age less than 45 yrs, baseline estimated creatinine clearance >90ml/min, and weight >55kg.
Hepatitis C antibody	Consider testing MSM every 12 months. Incident HCV infections have been reported among PrEP users who deny injection drug use.

The main side effect of TDF is renal impairment so close monitoring is required for clients with co morbid conditions like Diabetes Mellitus and uncontrolled Hypertension which affect the kidneys

PrEP COUNSELLING

Initial PrEP Counselling

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** of 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.**

Assess client's understanding that the protection provided by PrEP is not 100%.

Explain 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.

Follow up counselling

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** & **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.

ADHERENCE TO PREP

Adherence to drug(s) means that an individual is taking prescribed medications orrectly 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.

PrEP works when taken as prescribed; correctly and consistently!!!

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

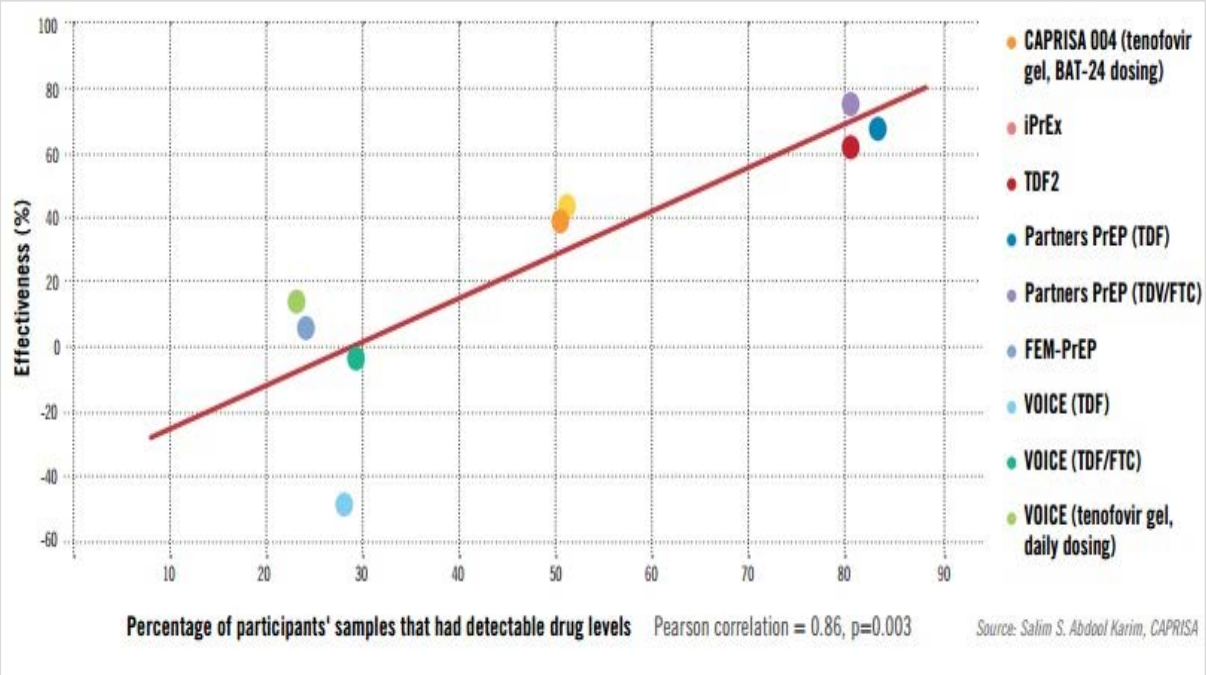
– Clinic and lab assessments.

– Drug collection/repeat prescription.

Truvada for PrEP provides 92%-99% reduction in HIV risk for HIV-negative individuals who take the pills every day as directed. If a daily dose is missed, the level of HIV protection may decrease

According to data analysis from the iPrEx study that found PrEP to be effective:

- For people who take 7 PrEP pills per week, their estimated level of protection is 99%.
- For people who take 4 PrEP pills per week, their estimated level of protection is 96%.
- For people who take 2 PrEP pills per week, their estimated level of protection is 76%.



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. The figure on the next slide summarizes results from the clinical trials to show that the higher the percentage of participant samples that had detectable PrEP drug levels, the greater the efficacy.

Common reasons for poor adherence

Discussion

What are the common reasons for poor adherence to medication e.g. ART?

Individual Factors	Medication Factors	Structural Factors
• 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	• Adverse events • Complexity of dosing regimens • Pill burden • Dietary restrictions (PrEP will require taking just one tablet daily and there are no dietary restrictions)	• 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 and Involuntary Non-Adherence

Voluntary Non-Adherence	Involuntary Non-Adherence
• Not convinced PrEP is needed • Does not believe PrEP works or is working • Does not like taking pills • Has experienced side-effects • Has experienced stigma while taking PrEP	• 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 mental illness • Can not afford PrEP (in settings where clients pay for PrEP services)

The role of health workers in adherence

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 users.

Adherence assessment methods

- 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*

Discussion

What are the advantages and disadvantages of each method?

Approaches to PrEP Medication Adherence Support

Support Issue:	Provider Options:

Adequate and accurate PrEP knowledge	• Briefly explain or provide materials about:
	  ○ 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	• 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.

Foster self-efficacy	• Foster discussion of personal perception of HIV risks.
	• Recommend or provide medication-adherence tools:
	  ○ Pill boxes
	  ○ Phone apps, pager, or SMS reminder services

Routinized daily schedule	• Discuss how to integrate daily dose with other daily events and what to do when away from home.

Support Issue:	Provider Options:
Provider support	• 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	• Discuss privacy issues for PrEP user. • Offer to meet with partners or family members if they are supportive.
Mental health and substance abuse	• Consider screening for depression or substance-abuse problems. • Provide or refer to indicated mental health or substance-abuse treatment and relapse-prevention services.
Population challenges	• Consider additional medication-adherence support for: ○ Adolescents. ○ People with unstable housing. ○ Transgender women. ○ Others with specific stressors that may interfere with medication adherence.

DISCUSSION

Discuss on strategies to support pill taking

- Schedule medication taking time to correspond with the patient's daily routine activities
- Use reminders e.g. cell phone, alarms, beepers, calendars
- Use of pillboxes like in figure X below
- Join an on-line support group e.g. Facebook: PrEP Rethinking HIV Prevention
- Review disclosure issues to identify those who can support the patient's intentions to take their pills or barriers to pill-taking due to lack of disclosure/privacy at home
- Use alternative methods of communication: SMS, social networking, mobile applications
- Collect additional contact information for each patient
- Integrate mobile services and outreach into existing services
- Enhance peer support strategies, such as the use of clubs

- Provide alternative clinic hours, if possible
- Provide patients in advance with referral partners in the event that they migrate, or provide with additional stock/prescription

PREP SIDE EFFECTS

Truvada for PrEP is generally safe and well tolerated. Most people on PrEP report experiencing no side effects, however some side effects were reported in clinical trials. Symptoms usually start in the first few days or weeks of PrEP, are usually mild and resolve without stopping PrEP.

Pharmacovigilance is the active surveillance and monitoring of adverse events (for initial roll-out). It should include:

- Creatinine test before initiation and for monitoring
- Random PK testing (to measure adherence)
- Learning from demonstration and funded projects

Frequent adverse events include:

Nausea: 9% of those who received Truvada reported nausea in the first month, compared with 5% of those who received placebo.

Headaches: 4.5% of participants who received Truvada reported headaches, compared with 3.3% of those who received placebo.

Weight loss: 2.2% of those who received Truvada reported unintentional weight loss of more than 5%, compared with 1.1% of placebo users

Small increases in serum creatinine: Truvada is known to cause small increases in serum creatinine, a naturally occurring molecule filtered by the kidneys. In this study, 0.3% of those who received Truvada experienced mild increases in serum creatinine that persisted until the next test. Creatinine levels went back down once these participants stopped taking PrEP. Four of the five participants restarted PrEP without recurrence of the creatinine increase. Investigators monitored kidney function throughout the study and found no serious problems.

Approximately 1 in every 200 PrEP users may develop an elevation of serum creatinine.

- Defined as a 50% increase above baseline or an elevation above the normal range.
- Reminder: 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.**

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 pre-eclampsia during pregnancy.

MODULE 4; SPECIAL CONSIDERATIONS FOR ADOLESCENT GIRLS AND YOUNG WOMEN

OBJECTIVES

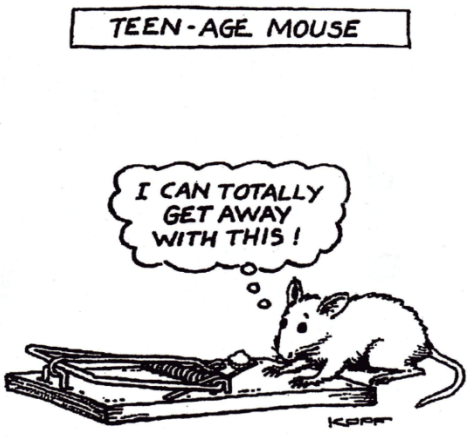
By the end of this training you will be able to:

- Identify the specific HIV and SRH needs of AGYW (ages 15-24)
- Understand key components of youth friendly SRH and combination HIV prevention service delivery, including oral PrEP services
- Understand which AGYW are most likely to benefit from oral PrEP (high risk and able to initiate and adhere)
- Initiate, monitor, and follow up AGYW on oral PrEP in youth friendly ways, responsive to their specific circumstances, and within a rights-based framework
- Provide and/or work with multiple cadres (e.g. CHWs, peers) to provide youth friendly oral PrEP adherence and counselling support

DEVELOPMENTAL CONSIDERATIONS – THE ADOLESCENT BRAIN

Adolescents are not mini adults…

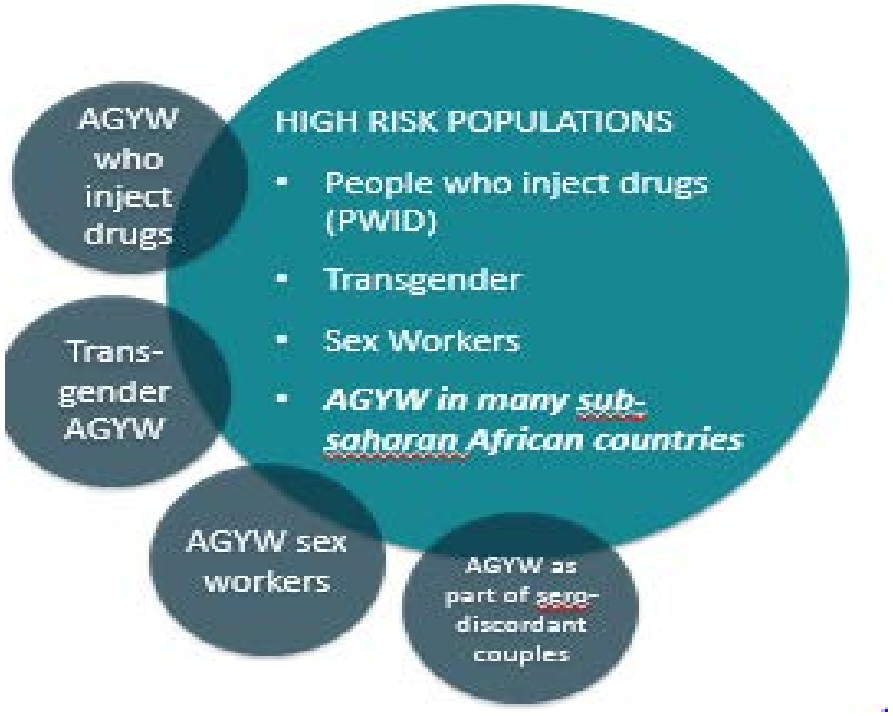
Less developed frontal lobe capacities for executive function, impulse control, and long-term decision-making. More developed limbic lobe favouring emotions, impulsive behaviour, and short-term gratification.



Adolescence is a time of physiological, sexual, and social changes: Changing bodies and hormones create sexual desire and focus on sex; Peer pressure is highly influential; a time of experimentation, testing limits, and questioning authority

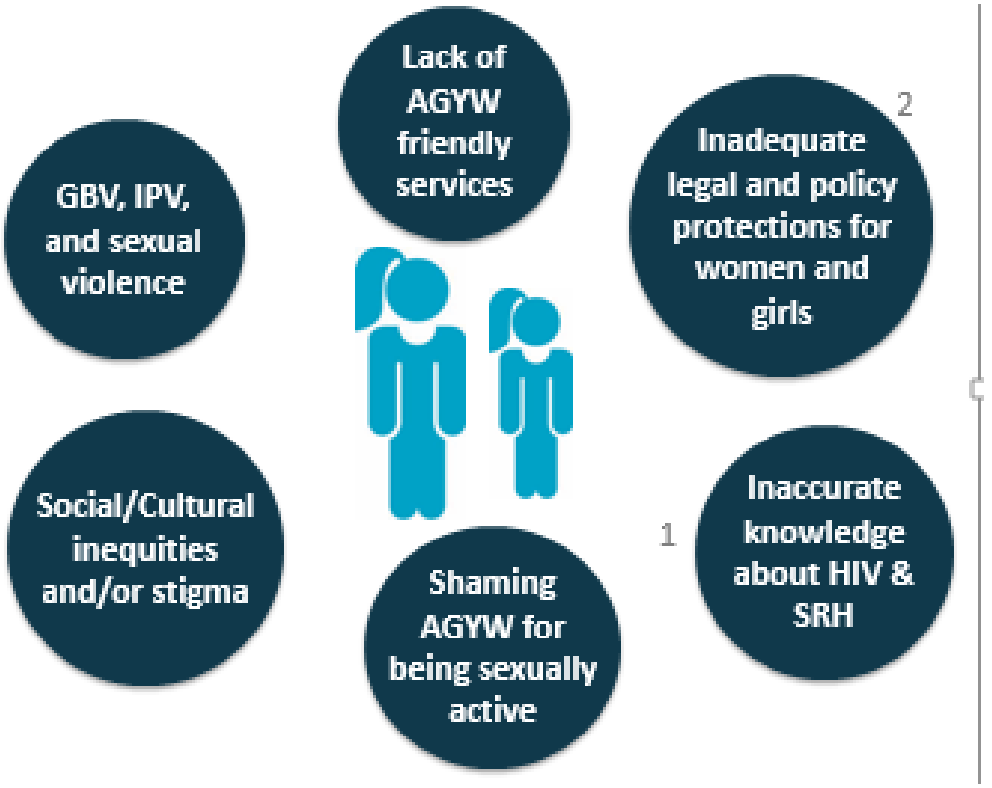
AGYW may also be…

- transgender
- with multiple sexual partners
- people who have an STI
- with partners who are HIV-positive or have unknown HIV status
- engaged in sex work



HIV in context – social and structural drivers

HIV among AGYW is fuelled by a combination of factors that create an environment of risk



Gender-based violence, particularly intimate partner and sexual violence, is widespread, greatly increasing risk of acquiring HIV. In some settings, up to 45% of adolescent girls report that their first sexual experience was forced. Globally, only 3 in every 10 adolescent girls and young women aged 15-24 years have comprehensive and accurate knowledge about HIV and other sexual and reproductive health issues.

SRH and HIV services are not generally friendly to the concerns and needs of AGYW, particularly for those who are unmarried. Lack of legal rights reinforce the subordinate status of women, including rights to divorce, to own and inherit property, to sue and testify in court, and to open bank accounts. Cultural constraints and/or stigma against AGYW for being sexually active outside of marriage can affect delivery of and access to SRH and HIV services for AGYW

Factors to Consider for AGYW

Risk factors	Protective factors
• **Poverty** • **Peer pressure** • **Sexual coercion** • **Transactional sex** • **Age-disparate relationships** • **Teenage pregnancy** • **Physiological vulnerability** • **Barriers to using health services** • **Dropping out of school** • **Being an orphan or in a child-headed household**	• **Youth-friendly services** • **Positive role models** • **Guidance and engagement on staying in school from trusted adults** • **Access to HIV prevention options**

Challenges and barriers to SRH and HIV services for AGYW

DISCUSSION

What are the key barriers for adolescents and youth accessing SRH and HIV services (from a client's perspective)?	What are the key challenges providing SRH and HIV services to AGYW (from a provider's perspective)?

Issues relating to access…

Inflexible and inconvenient clinic opening times

Clinic location, distance from home and availability, and the need for money for transport

Sitting in waiting rooms with adults, some of whom may know them

The attitude of staff – receptionists, clerks and nurses – who may be rude and judgmental

Nurses who may not give enough information or clarity; lack of confidentiality, privacy and sufficient time

The physical environment which looks intimidating, clinical and unattractive

Lack of accessible information developed to address the concerns, language and level of young people, which is easy to read and relevant to their lives

Issues related to quality of care…

Barriers relating to the quality of care which may discourage youth from using the clinic or completing treatment, e.g. drug stock-outs; having to walk through a waiting room with a urine sample; etc.

Anxiety about confidentiality and privacy

Issues related to communication… …

Impatient and unsympathetic staff who do not deal well with the embarrassment or problems young people encounter

Staff with poor listening skills

Embarrassment of provider who cannot discuss issues related to sexuality and safer sex

The language used and how well the health worker explains to the patient the nature of the problem and treatment

Client-related barriers	Community-related barriers	Provider-related barriers	Health system barriers	Product-related barriers
Don't know where to go Don't have resources to get to the service Staff attitude – judgmental, reprimanding Don't feel comfortable, embarrassed, scared to be seen by community Low self-esteem, stigma, shame, including self-stigma, self-shame Myths, misconceptions Lack of sexual partner support	Cultural, religious, moral perspectives Myths, misconceptions Community does not support the service	Young people do not use the service Young people are difficult Health care providers lack confidence to provide services to adolescents – especially uncomfortable discussing sex and sexuality Myths and misconceptions Overwhelming number of clients with special needs! – HIV, TB, elderly, babies, sex workers,	Legal, policy frameworks unclear, unsupportive Time of service: Can't get to the service because of school/work Lack of clear guidelines and protocols, not trained in the provision of SRH services Service unavailable, told to return Time constraints to provide adolescent friendly care, too many in the queue, over worked The commodities/supplies are not available There are no/few/inadequate referral agencies for youth	Unfavourable dosing schedules Unfavorable packaging, size, color of the product

		MSM, LGBTI, migrants, etc.		