PrEP Guidelines: SA HIV Clinicians Society
Ongoing HIV transmission despite expanding access to ART – SA

Treatment exposure has doubled from 16.6% in 2008 to 31.2% in 2012.

Source: HSRC, 2012
HIV PREVENTION TOOL-KIT

- Treatment for prevention
  - Donnell D, Lancet 2010
  - Cohen M, NEJM 2011

- Behavioural positive prevention
  - Fisher J, JAIDS 2004

- Oral pre-exposure prophylaxis
  - Grant R, NEJM 2010 (MSM)
  - Baeten J, 2011 (Couples)
  - Paxton L, 2011 (Heterosexuals)

- Post Exposure prophylaxis (PEP)
  - Scheckter M, 2002

- Male circumcision
  - Gray R, Lancet 2007

- Treatment of STIs
  - Grosskurth H, Lancet 2000

- Female Condoms

- Male Condoms

- HIV Counselling and Testing
  - Coates T, Lancet 2000

- Behavioural Intervention
  - Abstinence
  - Be Faithful

- Microbicides for women
  - Abdool Karim Q, Science 2010

- Vaccines
  - Rerks-Ngarm S, NEJM 2009

Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission.
PrEP works if you take it

Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection

Guidance on pre-exposure oral prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV: Recommendations for use in the context of demonstration projects

July 2012

Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV

US Public Health Service

Preexposure prophylaxis for the prevention of HIV infection in the United States - 2014
Southern African guidelines for the safe use of pre-exposure prophylaxis in men who have sex with men who are at risk for HIV infection

GUIDELINES

Southern African guidelines on the safe use of pre-exposure prophylaxis in persons at risk of acquiring HIV-1 infection

GUIDANCE ON PRE-EXPOSURE ORAL PROPHYLAXIS FOR SERODISCORDANT COUPLES AND WOMEN WHO HAVE SEX WITH MEN

Recommendations for use in the United States

July 2012

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014
What is PrEP?

- PrEP involves taking a pharmaceutical agent prior to an exposure to prevent an outcome
  - (e.g. infection by a microbe, such as malaria)
- HIV: ARV medications to prevent HIV infection
- TDF/FTC as FDC recommended
Indications for PrEP

PrEP should be considered for people who are HIV-negative and at significant risk of acquiring HIV infection

- Any sexually active HIV-negative *MSM or transgender person* who wants PrEP
- *Heterosexual women and men who want PrEP*
- People who inject *drugs*
- Include *adolescents and sex workers*
  - especially vulnerable: young MSM and adolescent girls
Contra-indications to PrEP

- HIV-1 infected or evidence of possible acute infection
- Suspicion of window period following potential exposure
- Adolescents <35 kg or <15 years who are not ≥Tanner stage 3
- Poor renal function (creatinine clearance <60 mL/min)
- Other nephrotoxic drugs (eg aminoglycosides)
- Unwilling or unable to return for 3-monthly visits
- Pregnant or breastfeeding women
Risk assessment

In the past six months:
1. Have you had sex with men, women or both?
2. How many men/women have you had sex with?
3. How many times did you have sex without a condom?
4. How many of your partners were HIV-positive or of unknown HIV status?
5. With these positive/unknown status partners, how many times did you have sex without wearing a condom?
Or more simply…

In the past six months:
1. Have you had sex?
2. Have you had unprotected (condom-less) sex?
3. Have you had sex with partners who are HIV-positive or whose HIV status you did not know?
4. Have you had sex under the influence of alcohol and/or drugs?
Or even more simply...

In the past six months:
1. Have you had sex?
2. Have you had unprotected (condom-less) sex?
Eligibility criteria

1. Anyone identified as being at high risk for HIV exposure
2. No contra-indications to FTC/TDF FDC
3. HIV-negative / not thought to be in the window period
4. Absence of symptoms of acute HIV infection
5. Willing and able to attend 3-monthly visits
6. Willing and able to adhere to PrEP (to take pills)
7. Understands that the protection provided by PrEP is not complete
8. Recurrent use of PEP
Starting PrEP

- Screening
- PrEP initiation visit
- One month follow-up
- Three-monthly maintenance visits
Screening visit

- Educate: risks and benefits of PrEP
- Assess risk and eligibility
- HCT/creatinine/HBV/STI screen/pregnancy
- Contraception/condoms/lube
- Arrange follow-up
Starting PrEP

**TABLE 1:** Mandatory baseline investigations for pre-exposure prophylaxis initiation.

<table>
<thead>
<tr>
<th>Screening</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>Laboratory ELISA preferably - fourth generation rapid if ELISA not available</td>
</tr>
<tr>
<td>Renal function</td>
<td>eGFR &gt; 60 mL/min</td>
</tr>
<tr>
<td>Hepatitis B screen</td>
<td>Surface antigen (HBsAg)</td>
</tr>
<tr>
<td></td>
<td>Antibody to surface antigen (HBsAb)</td>
</tr>
<tr>
<td>STI screen</td>
<td>Symptomatic screen</td>
</tr>
<tr>
<td></td>
<td>Examination if indicated</td>
</tr>
<tr>
<td></td>
<td>Urine dipstix for urethritis</td>
</tr>
<tr>
<td></td>
<td>Serological screening for syphilis (rapid or laboratory)</td>
</tr>
<tr>
<td></td>
<td>Full STI panel if resources allow</td>
</tr>
<tr>
<td>Pregnancy screen</td>
<td>Rapid pregnancy test or beta HCG</td>
</tr>
</tbody>
</table>
Managing abnormal screening results

- Abnormal renal function (CrCl <60 mL/min)
  - No PrEP
  - Recheck after 2 weeks – if normal can start PrEP
- HBV screening – see table
- Treat STIs as per national guidelines
Hepatitis B immune status and PrEP

**TABLE 3:** Hepatitis B immune status and pre-exposure prophylaxis eligibility.

<table>
<thead>
<tr>
<th>Hepatitis B surface antigen (HBsAg)</th>
<th>Hepatitis B surface antibody (HBsAb)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (-)</td>
<td>Negative (-)</td>
<td>Start PrEP, vaccinate concurrently</td>
</tr>
<tr>
<td>Negative (-)</td>
<td>Positive (+)</td>
<td>Start PrEP, no vaccine needed</td>
</tr>
<tr>
<td>Positive (+)</td>
<td>N/A</td>
<td>Refer for evaluation</td>
</tr>
</tbody>
</table>

N/A, not applicable; PrEP, pre-exposure prophylaxis.

- Acute/chronic HBV: LFT monitoring
PrEP initiation visit

- HCT
- Eligibility (incl labs and CrCl)
- HBV vaccination
- STI treatment
- Educate
- Contraception / condoms / lubricant
- TDF/FTC for one month
- Follow-up date

- PrEP side effects
- Acute HIV infection
- Bone health
- Effective use of PrEP
One month follow-up

- PrEP initiation visit PLUS:
- Tolerability / side effects
- Manage side effects
- Effective use

- Contraception / condoms / lubricant
- Creatinine clearance

- Labs
- 3 months TDF/FTC Follow-up
Maintenance visits

Repeat procedures done at one month

CrCl: at 4-month visit then 12-monthly

6-monthly STI screen incl urine dipstix and rapid syphilis

Complete HBV immunisation at 6 months
Risks and side effects

- GI effects
- ARV resistance
- HBV management
- Renal
- BMD
- Risk compensation
Resistance

- Resistance has occurred rarely when PrEP initiated during acute HIV infection
  - M184V
- Prevent by not initiating/re-initiating PrEP during acute HIV infection
- HIV testing
  - 3-monthly
  - symptoms viral illness
  - before resuming PrEP
  - accompanied by HIV exposure assessment, symptom screen and targeted examination
Side effects

- Mild: headache, malaise

- GI side effects
  - Nausea, weight loss

- Renal toxicity
  - Transient increases in serum creatinine
  - Decreased GFR

- Decreased BMD
  - Less cf HIV-infected individuals on TDF
  - No differences in fracture rates
HBV management

- Risk of viral rebound in undiagnosed chronic HBV if PrEP stopped
- Screen for HBsAg and HBsAb
- HBV vaccination if HBsAg+/HBsAb- 
  - Require additional LFT monitoring
- PrEP not contra-indicated in HBV infection
  - Require additional LFT monitoring
- Check LFT after stopping PrEP in chronic HBV
Stopping PrEP

- Positive HIV test
- Request of user
- Safety concerns
  - Creatinine clearance <60 mL/min
- Risks outweigh benefits
Cycling on and off PrEP

When starting
- For anal sex: 7 days of daily TDF/FTC to reach adequate tissue levels
- For vaginal sex: 20 days
- Use other methods of protection

When stopping
- Continue PrEP for 28 days after last potential HIV exposure
Full of little gifts

**BOX 4:** What if users ask about stopping condom use while on prophylaxis?

1. Do not be judgemental about patient preference.
2. Explain that this is a valid choice because of potentially negative consequences.
3. Stress that PrEP prevents HIV.
4. Stress that PrEP prevents HIV.
5. Confirm a regular and adequate management plan.
6. Confirm an acceptable contraception plan where indicated.
7. Address vaccine-preventable STIs, e.g. hepatitis A and B and HPV.
What if user asks about stopping condom use?

1. Do not be judgemental
2. Explain that this is a valid choice but…
   - PrEP prevents HIV but not STIs
   - PrEP prevents HIV but not pregnancy
3. Regular STI screening and management plan
4. Effective and acceptable contraception plan where indicated
5. Vaccinate against all vaccine-preventable STIs, e.g. hepatitis A and B and HPV where possible
Full of little gifts

BOX 4: What if users ask about stopping condom use while on pre-exposure prophylaxis?
1. Do not be judgemental about patient preferences.
2. Explain that this is a valid choice but there are potentially negative consequences.
3. Stress...

BOX 5: 'Adherence' versus 'effective use'.

These guidelines use the term 'effective use' in place of adherence. Adherence is often understood by healthcare workers to mean taking ARV treatment adherence, as life-long drug adherence is necessary to ensure viral suppression. Oral PrEP must be taken daily, and during times of HIV exposure risk, although there are several instances where less than perfect adherence is still highly effective. For example, if times when it would be appropriate to cycle off oral PrEP while MSM move out of 'seasons of risk', or when female sex workers travel home to visit family, taking a break from sexual activity

Consistent use of oral PrEP is measured with the same standards as ARV treatment adherence, it may show up as lacking, but the ARV population at risk has used the drug effectively. The term 'effective use' only comes into play when discussing whether ARV-based prevention has been used properly; this is akin to 'effective use of condoms' as we seldom talk about non-adherence.
Full of little gifts

**BOX 4:** What if users ask about stopping condom use while on pre-exposure prophylaxis?

1. Do not be judgemental about patient preferences.

2. **BOX 5:** ‘Adherence’ versus ‘effective use’.

These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed. These guidelines use the term ‘effective use’ rather than ‘adherence’. Adherence often refers to treatment support, but not necessarily the success of the intervention. Therefore, adherence is still needed.

**BOX 6:** Tips to support effective use.

Include user-focused effective use strategies for each contact. Provide a clear explanation of the benefits of effective use and consider a neutral manner, asking if the user has any challenges that might be making PrEP difficult. Also explore possible facilitators to pill use, in three identified facilitators when developing strategies to improve:

**1.** Daily pill taking:

- **Wearers** (cellphone, alarm clock, diary, partner reminder).
- **With daily activity** (breakfast, brushing teeth).
- **Use a pillbox.**
  - Food is **NOT** required for pill taking.
  - Join an on-line support group, e.g. Facebook: PrEP Rethinking HIV Prevention or #wethebrave.
And the gifts keep coming

**BOX 7: Strategies to reduce the likelihood of antiretroviral resistance.**

Feasibly exclude acute HIV infection before initiating PrEP by:

- conducting antibody HIV testing before commencing or re-prescribing PrEP
- enquiring about pill taking patterns and whether any pills were missed
- among persons with a negative HIV antibody test, screen to detect signs and symptoms of acute HIV (e.g., fever, sore throat, rash, joint pain, cough in the 2-4 weeks preceding examination (temperature, ENT and skin examination text box)
- considering time period between exposure and window period of tests being used
- If symptoms or signs of acute HIV are identified:
  - At screening: symptoms subside and rapid antibody test remains negative: continue PrEP
  - At screening: symptoms subside and rapid antibody test remains positive or follows up until follow-up HIV antigen/antibody testing is negative: continue PrEP while awaiting results of follow-up HIV antibody testing (2-4 weeks) or may decide to withhold PrEP if tests available
- Note: if PrEP has been taken consistently, breakthrough infection is unlikely. Withholding PrEP may put an effective user at greater risk for HIV acquisition
- Support client to maximise effective use and include effective use counselling at each visit
- Stop PrEP should requirements for PrEP eligibility not be fulfilled or if client recognises risk profile has altered or wishes to use a different combination of prevention
- Counsel client that recommencement will require all of the above steps again.
Exclude acute HIV infection

- HIV test before commencing or restarting PrEP
- Ask about missed doses
- Negative HIV test
  - Clinical screen for symptoms acute HIV
  - Targeted examination
- Time between last potential exposure and window period of tests used
Exclude acute HIV infection

If symptoms/signs of acute HIV:
  
  o At screening
    – Postpone PrEP until symptoms resolve AND
    – Follow-up test 2-4 weeks later is negative
  
  o At follow-up
    – Continue PrEP while awaiting results of HIV test
    – OR withhold PrEP until results available
    – If PrEP taken consistently, breakthrough infection is unlikely – may put user at risk by withholding
Exclude acute HIV infection

- Support maximum effective use
  - Counselling at each visit
- Stop PrEP appropriately
- Counsel about steps required if restart PrEP
And the gifts keep coming

<table>
<thead>
<tr>
<th>BOX 7: Strategies to reduce the likelihood of antiretroviral resistance.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feasibly exclude acute HIV infection before initiating PrEP by:</td>
</tr>
<tr>
<td>conducting antifilarial therapy;</td>
</tr>
<tr>
<td>enquiring about sexual history, and HIV status of sexual partners;</td>
</tr>
<tr>
<td>conducting serological testing for HIV;</td>
</tr>
<tr>
<td>among persons who have sex with persons who are HIV-positive.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BOX 8: Acute HIV-infection.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of the syndrome ranges from mild non-specific ‘viral’ symptoms to a severe infectious mononucleosis-like illness with lymphadenopathy, fever, rash, and transient profound CD4 depletion.</td>
</tr>
</tbody>
</table>

**Symptom:**
- malaise
- anorexia
- myalgias
- headache
- sore throat
- sore glands
- rash.

**Sign:**
- fever
- lymphadenopathy
- myalgias
- inflamed pharyngitis
- oral herpetic ulceration
- papular rash (maculopapular or urticarial)
- viral meningitis
- Guillain-Barre syndrome
- *Pneumocystis* pneumonia
- cryptococcal meningitis
- oral/oesophageal candidiasis.
## Common symptoms and signs of acute HIV infection

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>malaise</td>
<td>fever, sweating</td>
</tr>
<tr>
<td>anorexia</td>
<td>generalised lymphadenopathy</td>
</tr>
<tr>
<td>myalgia</td>
<td>hepatosplenomegaly</td>
</tr>
<tr>
<td>headache</td>
<td>non-exudative pharyngitis</td>
</tr>
<tr>
<td>sore throat</td>
<td>orogenital herpetiform ulceration</td>
</tr>
<tr>
<td>sore glands</td>
<td>truncal rash (maculopapular or urticarial)</td>
</tr>
<tr>
<td>rash</td>
<td>viral meningitis Guillian-Barre syndrome</td>
</tr>
</tbody>
</table>

- Generalised lymphadenopathy
- Hepatosplenomegaly
- Non-exudative pharyngitis
- Orogenital herpetiform ulceration
- Truncal rash (maculopapular or urticarial)
- Viral meningitis

Guillian-Barre syndrome
And the gifts keep coming
HIV prevention methods

Biomedical
- condoms and lubricants
- frequent HIV testing
- early access to ART
- PEP and PrEP
- VMMC
- STI screening and treatment
- needle syringe exchange and opioid substitution therapy for PWID

Psychosocial
- education: risk and safer sex
- HIV counselling and screening
- reducing no. of sex partners
- reducing alcohol and substance abuse
- addressing mental health
- couple counselling/programming
- harm reduction counselling and support for clients who use drugs
What about pregnancy and breastfeeding?

- Risk of seroconversion during conception and pregnancy
- Limited data regarding safety of PrEP for foetus
  - RCTs excluded pregnant women
  - Demonstration projects will provide some data
- APR: no evidence adverse outcomes in infants exposed to TDF/FTC ART
In SA: TDF/FTC PrEP CI in pregnant or breastfeeding women
Some final thoughts

- PrEP is seasonal
- PrEP isn’t for everyone
- PrEP use requires commitment
- Role of PrEP in serodiscordant couples
- Risk reduction counselling
- PrEP users are NOT patients
Acknowledgements

- SA HIV Clinicians Society
- PrEP guideline writing group