Southern African HIV Clinicians Society
3rd Biennial Conference
13 - 16 April 2016
Sandton Convention Centre
Johannesburg

Our Issues, Our Drugs, Our Patients

www.sahivsoc.org
www.sahivsoc2016.co.za
Sticking to guidelines:
PrEP guidelines

Michelle Moorhouse
15 Apr 2016
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
ABSTINENCE  CONDOMS  BEING FAITHFUL
**HIV PREVENTION TOOL-KIT**

- **Microbicides for women**
  - Abdool Karim Q, Science 2010

- **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

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

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

- **Vaccines**
  - Rerks-Ngarm S, NEJM 2009

- **Behavioural Intervention**
  - Abstinence
  - Be Faithful

**Note:** PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included — this is focused on reducing sexual transmission.
GUIDELINES

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 on the safe use of pre-exposure prophylaxis in persons at risk for HIV infection

July 2012

GUIDELINES

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
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). PrEP for
• HIV: ARV medications to prevent HIV infection
Indications for PrEP

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

1. any sexually active HIV-negative *MSM or transgender person* who wants PrEP
2. *heterosexual* women and men who want PrEP
3. people who inject *drugs*
4. include *adolescents and sex workers*
   – especially vulnerable: young MSM and adolescent girls.
Contra-indications to PrEP

1. HIV-1 infected or evidence of possible acute infection
2. suspicion of window period following potential exposure
3. adolescents <35 kg or <15 years who are not ≥Tanner stage 3
4. poor renal function (creatinine clearance <60 mL/min)
5. other nephrotoxic drugs (eg aminoglycosides)
6. unwilling or unable to return for 3-monthly visits
7. pregnant or breastfeeding women
Risk assessment

In the past 6 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 3/6 months:

1. Have you had sex within the past three months?
2. Have you had unprotected (condomless) 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?
Eligibility criteria

• Anyone identified as being at high risk for HIV exposure
• No contraindications to FTC/TDF FDC
• HIV-negative / not thought to be in the window period
• Absence of symptoms of acute HIV infection
• Willing and able to attend 3-monthly visits
• Understands that the protection provided by PrEP is not complete
• Recurrent use of PEP
Starting PrEP

Screening

PrEP initiation visit

One month follow up

Three monthly maintenance visits
## Screening visit

<table>
<thead>
<tr>
<th>Activity</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educate about the risks and benefits of PrEP</td>
<td></td>
</tr>
<tr>
<td>Assess risk and eligibility</td>
<td></td>
</tr>
<tr>
<td>Conduct HIV counselling and testing, serum creatinine level, hepatitis B and STI screen, pregnancy test</td>
<td></td>
</tr>
<tr>
<td>Contraceptive counselling and offer services (including condoms and lubricant)</td>
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<tr>
<td>Arrange follow-up visit</td>
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</tbody>
</table>
# 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>
## PrEP initiation visit

- Conduct HIV counselling and testing
- Confirm eligibility (including investigation results and creatinine clearance)
- Commence hepatitis B vaccination if indicated
- Provide STI treatment if indicated
- Educate client about PrEP side-effects and management
- Educate client about signs and symptoms of acute HIV infection
- Discuss behaviours that promote bone health, such as weight-bearing exercise and avoiding alcohol, tobacco and recreational drugs
- Initiate a medication effective use plan
- Provide condoms and lubricant
- Contraceptive counselling and offer services
- Provide one-month TDF/FTC (FDC) prescription and follow-up date
One month follow up

**PrEP initiation visit, PLUS:**

- Assess tolerability, side-effects and effective use
- Actively manage side-effects
- Measure serum creatinine and calculate creatinine clearance
- Contraceptive services
- Provide three-month TDF/FTC (FDC) prescription and follow-up date
Maintenance visits

Repeat procedures done at one-month follow-up

Measure serum creatinine and calculate creatinine clearance at four-month follow-up, and 12-monthly thereafter

Conduct 6-monthly STI screen, including urine dipstix and rapid syphilis test

Complete hepatitis B immunisation at 6 months
Risks and side effects

- GI effects
- ARV resistance
- Renal management
- HBV
- BMD
- Risk compensation
Stopping PrEP

1. Positive HIV test
2. Request of user
3. Safety concerns
   - Creatinine clearance <60 mL/min
4. 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 prophylaxis?

1. Do not be judgemental about patient preference.
2. Explain that this is a valid choice but be open about any negative consequences.
3. Stress that PrEP prevents HIV.
4. Stress that PrEP prevents sexually transmitted infections (STIs).
5. Confirm a regular condom management plan.
6. Confirm a qualitative contraceptive plan where indicated.
7. Encourage vaccine-preventable STIs, e.g. hepatitis A and B and HPV
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
4. Stress
5. Confirm
6. Confirm
7. Vaccinate

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

These guidelines use the term ‘effective use’ as a loose approximation of adherence. Adherence is often understood by healthcare providers as a word applied to ARV treatment adherence, as life-long intervals to ensure viral suppression. Oral PrEP must be adhered to, although there are periods less than perfect adherence is still highly effective in protecting against HIV. It’s when it would be appropriate to cycle off oral PrEP, when people move out of ‘seasons of risk’, or when female people might have time to visit family, taking a break from sexual activity. The current use of oral PrEP is measured with the same intervals as ARV treatment adherence, it may show up as lacking, but this is akin to ‘effective use of condoms’ as we seldom talk about 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'.
3.  
4.  
5.  
6.  
7.  

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

Include user-focused effective use routines to complement contact. Provide a clear explanation of the benefits of PrEP and convey the neutral manner, ask if the user has any challenges that make taking PrEP difficult. Also explore possible internal and external facilitators to pill taking and any barriers to effective use. Some tips to support effective use:

- **Option 1:** Pill taking:
  - Use daily habits (phone, alarm clock, diary, partner reminder).
  - Link with daily activity (breakfast, brushing teeth).
- **Option 2:** Pill taking and sex:
  - Use of condoms 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

<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 antibody HIV testing before commencing or re-prescribing</td>
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<tr>
<td>• enquiring about pill taking patterns and whether any pills were</td>
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<tr>
<td>among persons with a negative HIV antibody test, a rapid test to</td>
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<tr>
<td>screen to detect signs and symptoms of acute HIV infection (fever,</td>
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<tr>
<td>sore throat, rash, joint pain, cough in acute illness, chest</td>
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<tr>
<td>examination (temperature, ENT and chest examination) in consented</td>
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<tr>
<td>text box)</td>
</tr>
<tr>
<td>• considering time period between last sexual contact and window</td>
</tr>
<tr>
<td>period of tests being used</td>
</tr>
<tr>
<td>• If symptoms or at-risk behaviour suggest the possibility of acute</td>
</tr>
<tr>
<td>HIV infection, consider:</td>
</tr>
<tr>
<td>• At screening:</td>
</tr>
<tr>
<td>• If symptoms of acute HIV infection subside and rapid antibody test</td>
</tr>
<tr>
<td>remains positive then delay PrEP until follow-up HIV antigen/antibody</td>
</tr>
<tr>
<td>test is negative again or continue PrEP while awaiting results of</td>
</tr>
<tr>
<td>follow-up rapid antibody testing (2–4 weeks) or may decide to</td>
</tr>
<tr>
<td>withhold PrEP until results available</td>
</tr>
<tr>
<td>• If PrEP has been taken consistently, breakthrough infection is</td>
</tr>
<tr>
<td>unlikely. Withholding PrEP may put an effective user at greater risk</td>
</tr>
<tr>
<td>for HIV acquisition</td>
</tr>
<tr>
<td>• Support client to maximise effective use and include effective</td>
</tr>
<tr>
<td>use counselling at each visit</td>
</tr>
<tr>
<td>• Stop PrEP should requirements for PrEP eligibility not be fulfilled</td>
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<tr>
<td>or if client recognises risk profile has altered or wishes to use</td>
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<tr>
<td>a different combination of prevention</td>
</tr>
<tr>
<td>• Counsel client that recommencement will require all of the above</td>
</tr>
<tr>
<td>steps again.</td>
</tr>
</tbody>
</table>
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 antiretroviral treatment
  - enquiring about risk factors
  - among persons who may be at risk of HIV infection
  - examination
  - considering results of voluntary testing
  - If symptoms or signs remain negative
  - At screening:
  - (2-4 weeks) before initiating PrEP
  - At follow-up:
  - HIV antigen/antibody test
  - Note that, if negative, unlikely with acquisition

**BOX 8: Acute HIV-infection.**

Severity of the syndrome ranges from mild non-specific “viral syndrome” to a severe infectious mononucleosis-like illness with dysregulation and transient profound CD4 depletion.47-49

**Symptom:**
- malaise
- anorexia
- myalgias
- headache
- sore throat
- rash
- glandular

**Sign:**
- Lymphadenopathy
- Pharyngitis
- Herpetic ulcers
- Oral rash (maculopapular or urticarial)
- Viral meningitis
- Guillain-Barré syndrome
- Pneumocystis pneumonia
- Cryptococcal meningitis
- Oral/oesophageal candidiasis.
And the gifts keep coming

BOX 7: Strategies to reduce the likelihood of antiretroviral resistance.
- conducting antibody tests
- enquiring about pill testing
- among persons with symptoms to screen to detect signs of HIV infection: fever, sore throat, rash, lymphadenopathy
- considering time period of tests being done
- If symptoms or signs:
  - At screening: post-test counseling: remains negative
  - At screening: do not offer
  - At follow-up: may still HIV antigen/antibody test with follow-up test
  - Note that HIV likely unlikely: withholding acquisition
- Support client to make each visit
- Stop PrEP should recognise's risk profile
- Counsel client that

BOX 8: Acute HIV-infection.
- Severity of the syndrome ranges from mild non-specific symptoms to a more severe clinical course

BOX 9: HIV prevention for pre-exposure prophylaxis users.

General factors to consider:
- accessibility of condoms and compatible water-based lubricants
- no single HIV risk reduction intervention is likely to be effective
- combinations of prevention options, tailored to the client
- prevention options are likely to vary by context

Biomedical:
- male or female condom
- access to free condoms
- early antiretroviral treatment
- post-exposure prophylaxis

Surgical:
- circumcision
- removal of topical transmitters

Hormonal:
- progesterone-containing contraceptives

Social:
- education: risk and safer sex practices
- regular HIV counselling and screening
- reducing number of sex partners
- reducing alcohol and substance abuse
- addressing mental health needs
- couple counselling and 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 to TDF/FTC ART
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
• Francois Venter
• PrEP guideline writing group