

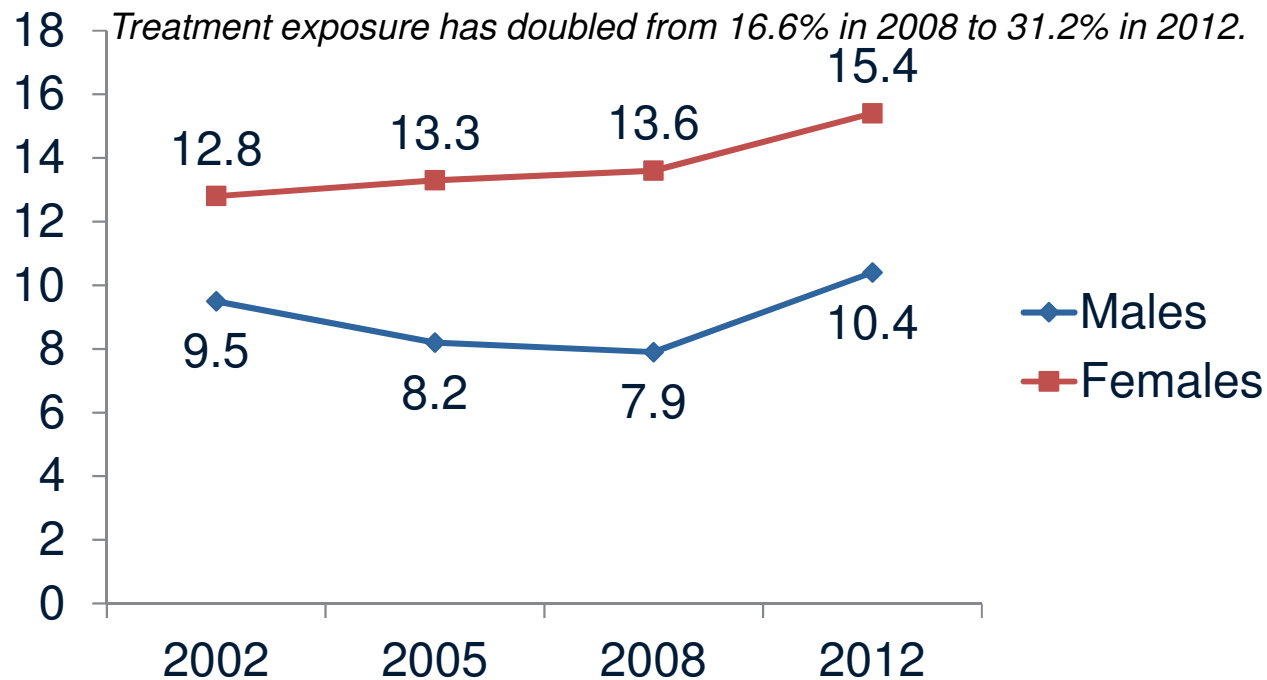


SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

# PrEP Guidelines: SA HIV Clinicians Society

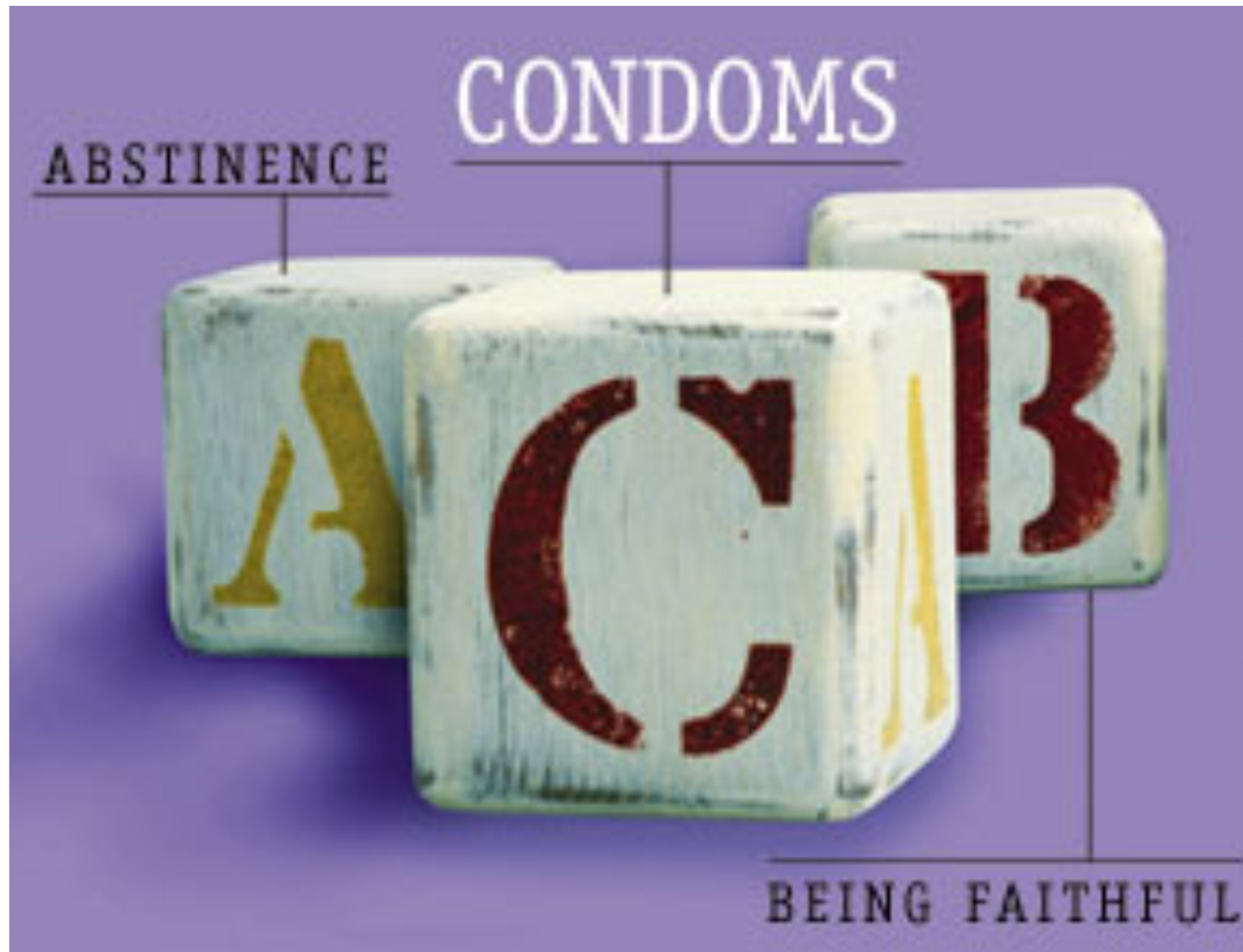


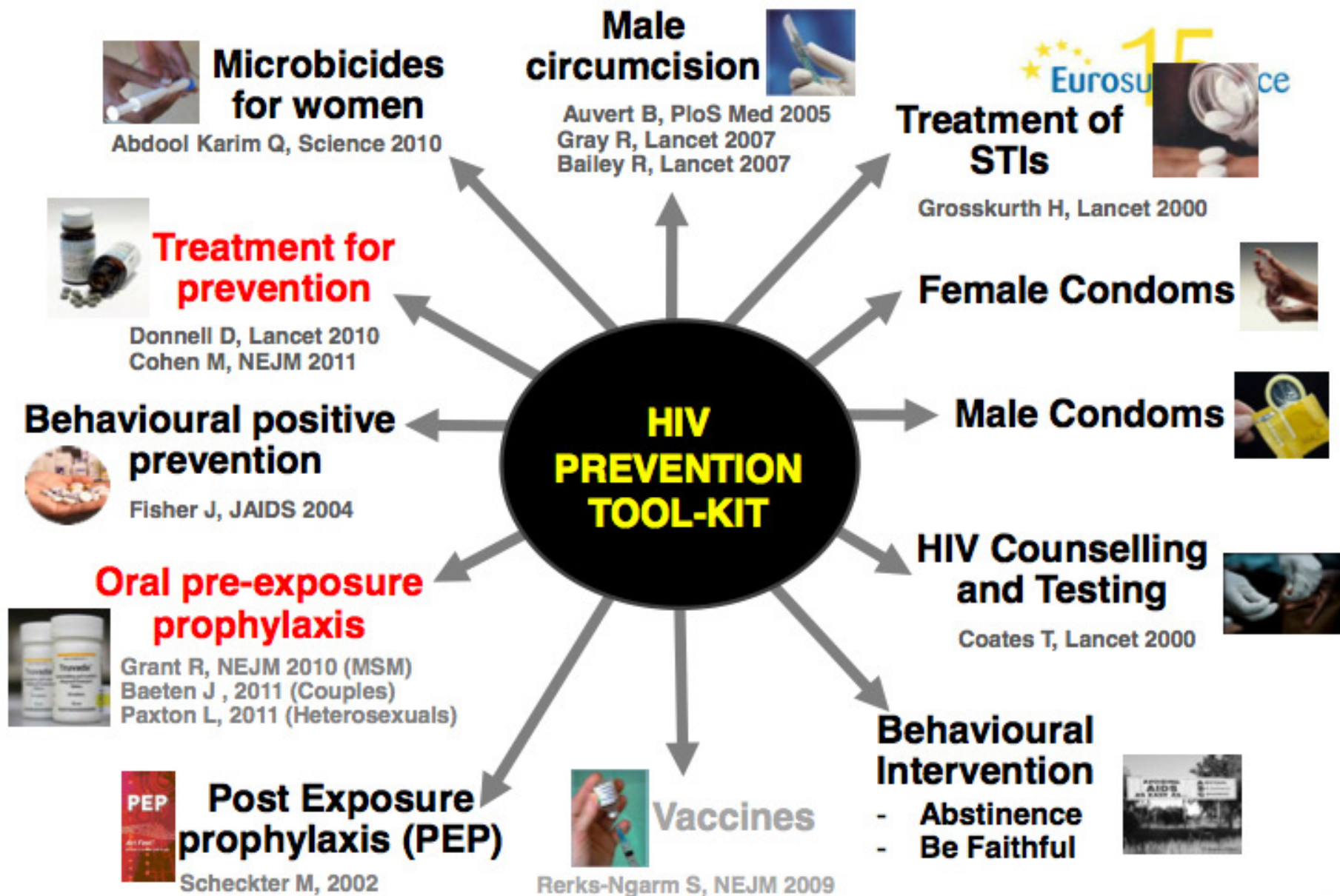
# Ongoing HIV transmission despite expanding access to ART – SA



Source: HSRC, 2012

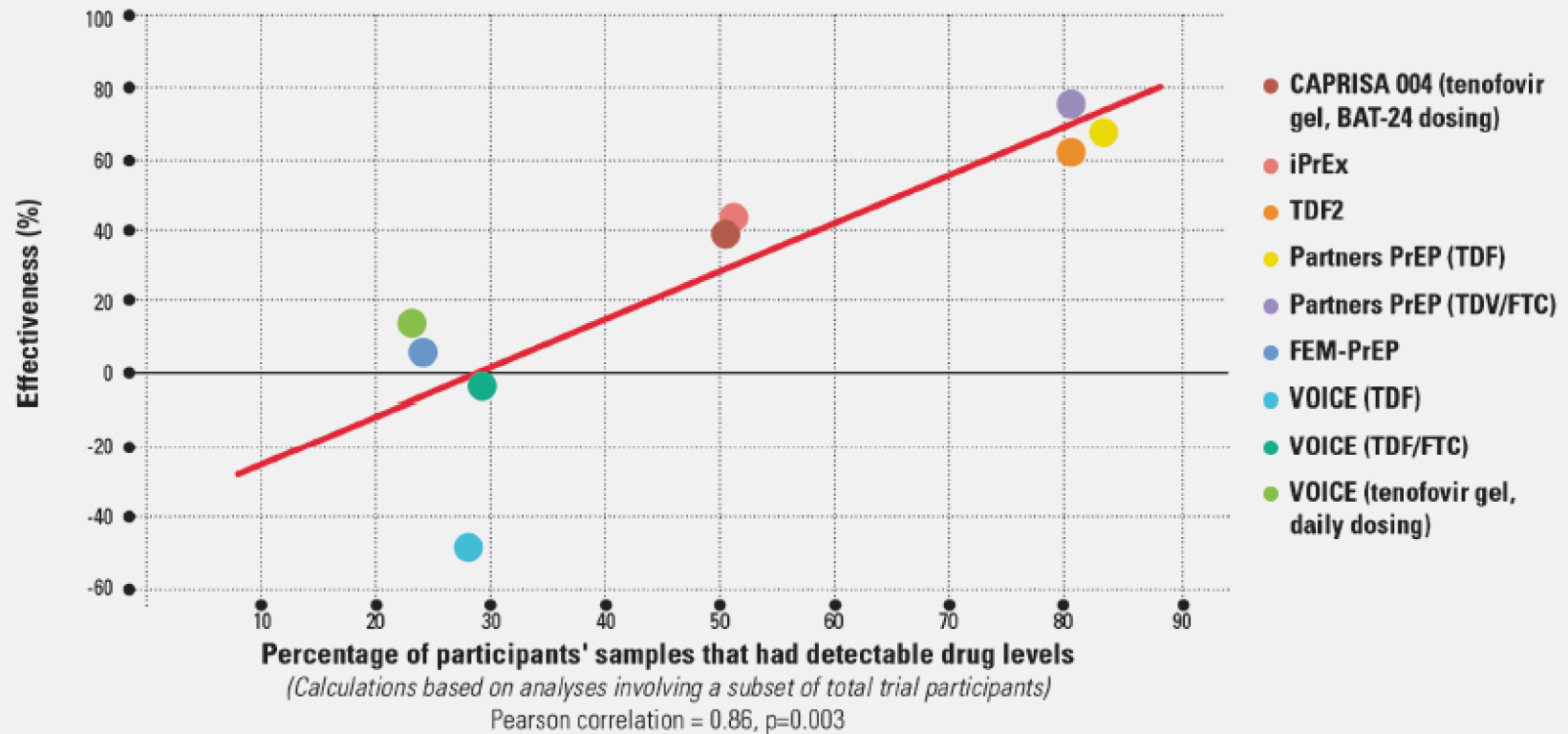






*Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, etc. have not been included – this is focused on reducing sexual transmission*

# 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.

Source: Salim S. Abdool Karim, CAPRISA





## **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



World Health  
Organization

## **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**



## **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**

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Recommendations for use in the

July 2012

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

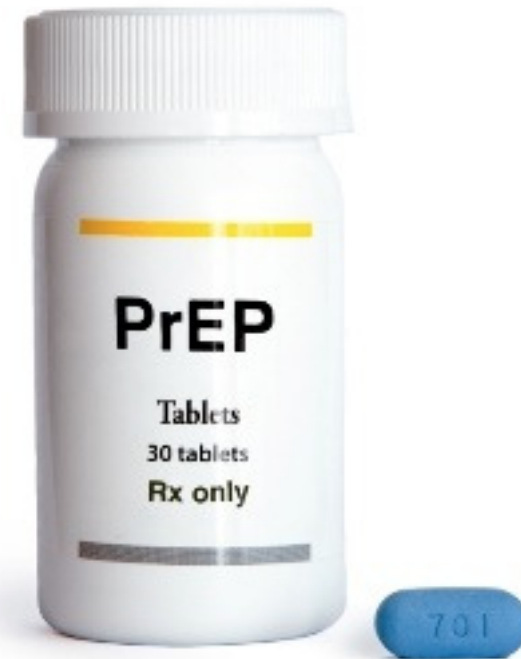
GENERAL  
THERAPY AND  
PRE-EXPOSURE  
PROPHYLAXIS FOR HIV

US Public Health Service

**PREEXPOSURE PROPHYLAXIS  
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# 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  $\geq$ 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.

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

# 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.

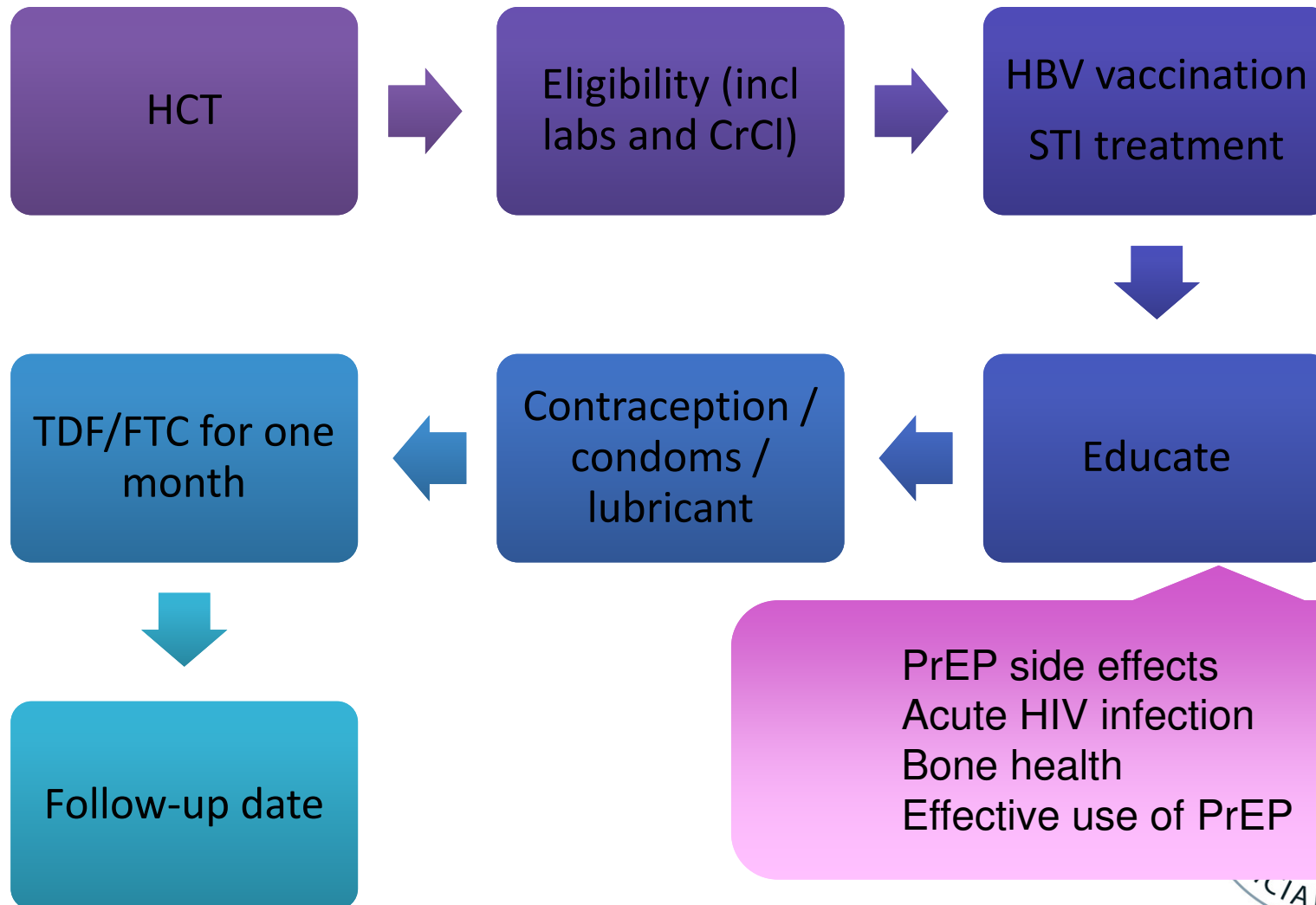
Hepatitis B surface antigen (HBsAg)	Hepatitis B surface antibody (HBsAb)	Action
Negative (-)	Negative (-)	Start PrEP, vaccinate concurrently
Negative (-)	Positive (+)	Start PrEP, no vaccine needed
Positive (+)	N/A	Refer for evaluation

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

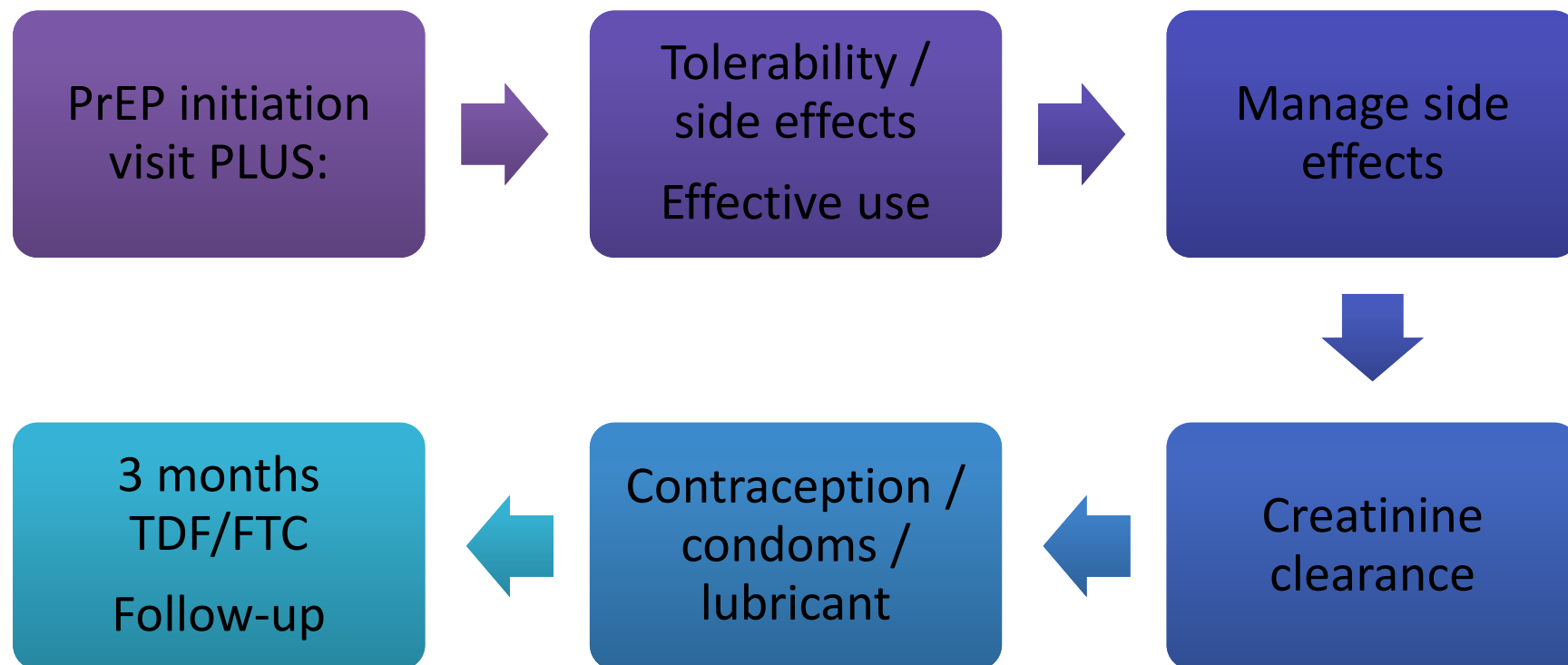
- Acute/chronic HBV: LFT monitoring



# PrEP initiation visit



# One month follow-up



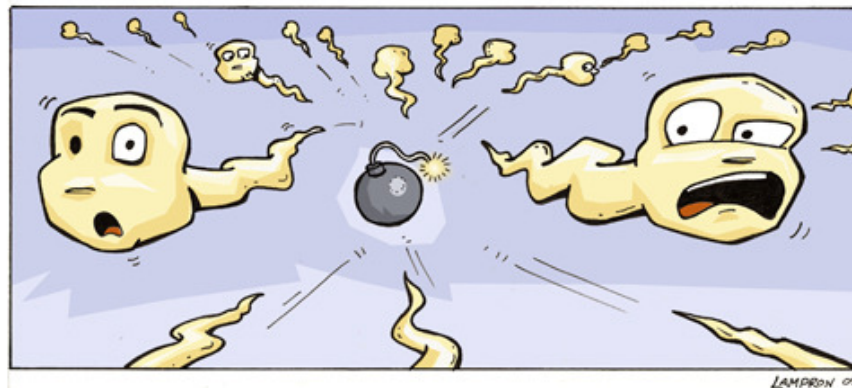
# Maintenance visits

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

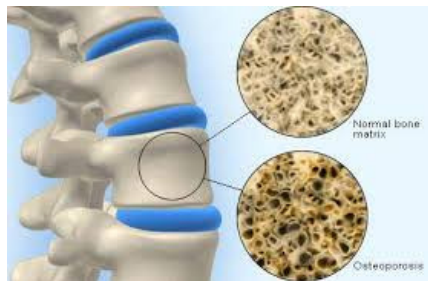


**HBV  
management**

**Renal**

**GI  
effects**

**ARV  
resistance**



**BMD**

**Risk  
compensation**





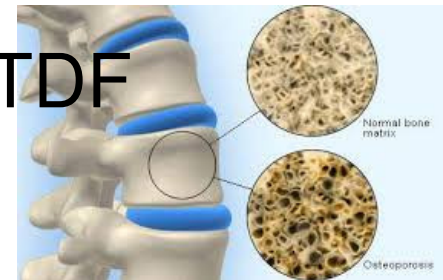
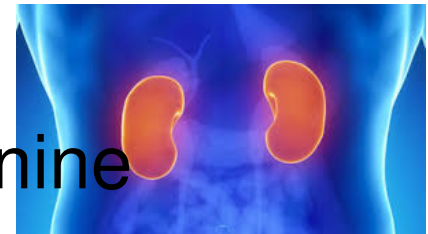
# Resistance

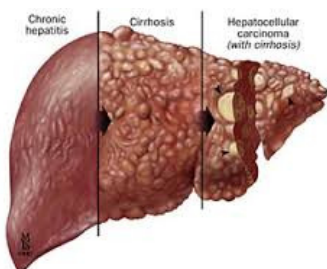
- Resistance has occurred rarely when PrEP initiated during acute HIV infection
  - M184V
- Prevent by not initiating/re-initiating PrEP during acute HIV infection
- HIV testing
  - 3-monthly
  - symptoms viral illness
  - before resuming PrEP
  - accompanied by HIV exposure assessment, symptom screen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





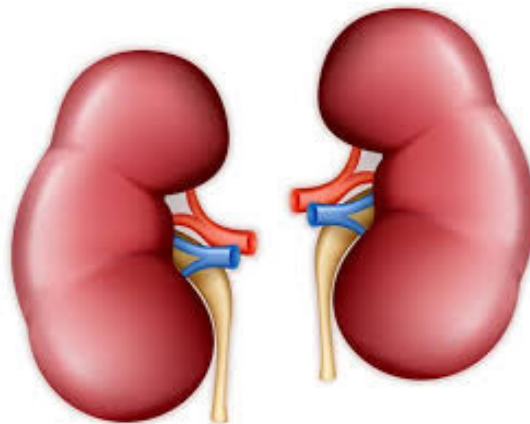
# HBV management

- Risk of viral rebound in undiagnosed chronic HBV if PrEP stopped
- Screen for HBsAg and HBsAb
- HBV vaccination if HBsAg+/HBsAb-
- 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 PrEP?

1. Do not be judgemental about patient preference.
2. Explain that this is a valid choice but discuss the potential negative consequences.
3. Stress that PrEP prevents HIV.
4. Stress that PrEP prevents other STIs.
5. Confirm a regular management plan.
6. Confirm a reliable contraception plan where indicated.
7. Discuss 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 that PrEP is not a substitute for condoms.
4. Stress that PrEP is not a substitute for condoms.
5. Confirm that the user understands the risks of stopping condom use.
6. Confirm that the user understands the risks of stopping condom use.
7. Vaccinate where appropriate.

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

These guidelines use the term 'effective use' rather than 'adherence'. Adherence is often understood by healthcare workers as a person's ability to follow instructions. When applied to ARV treatment adherence, as life-long adherence is required to ensure viral suppression. Oral PrEP must be taken consistently at regular intervals during times of HIV exposure risk, although there are some situations where less than perfect adherence is still highly effective. For example, a person may stop taking PrEP during times when it would be appropriate to cycle off oral PrEP, such as when MSM move out of 'seasons of risk', or when female sex workers return home to visit family, taking a break from sexual activity. Consistent use of oral PrEP is measured with the same standard as ARV treatment adherence, it may show up as lacking, but the population at risk has used the drug effectively. The term 'effective use' is used to when discussing whether ARV-based prevention has been used consistently; this is akin to 'effective use of condoms' as we seldom talk about condom 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

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

Include user-focused effective use tips at each contact. Provide a clear explanation of the benefits of PrEP. In a neutral manner, ask if the user has any challenges that are making PrEP difficult. Also explore possible facilitators to pill taking. Identify facilitators when developing strategies to improve PrEP use.

**PrEP daily pill taking:**

• Use reminders (cellphone, alarm clock, diary, partner reminder).

• Link pill taking 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.



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

**Feasibly exclude acute HIV infection before initiating PrEP by:**

- 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, re-screen to detect signs and symptoms of acute HIV infection (fever, sore throat, rash, joint pain, cough in the past 4 weeks) and a physical examination (temperature, ENT and skin examination) (infection text box)
  - considering time period between exposure and window period of tests being used
  - If symptoms or signs are present, consider:
    - At screening, if symptoms subside and rapid antibody test remains negative, follow-up
    - At follow-up, if symptoms persist, continue PrEP while awaiting results of follow-up antibody testing (2–4 weeks) or may decide to withhold PrEP until rapid tests available
  - Note that, 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:

- At screening
  - Postpone PrEP until symptoms resolve AND
  - Follow-up test 2-4 weeks later is negative
- 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

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

**Feasibly exclude acute HIV infection before initiating PrEP by:**

- conducting antiretroviral (ARV) tests
- enquiring about symptoms
- among persons screened to detect fever, sore throat, examination (text box)
- considering time period of tests taken
- If symptoms or signs:
  - At screening: remains negative
  - At screening: (2–4 weeks) confirmed
  - At follow-up: HIV antigen/antibody until follow-up
  - Note that, if unlikely. With acquisition
- Support client to each visit
- Stop PrEP should recognise risk
- Counsel client to

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

Severity of the syndrome ranges from mild non-specific 'viral' symptoms to a severe infectious mononucleosis-like illness with dysregulation and transient profound CD4 depletion.<sup>47,48</sup>

**Symptom:**

- malaise
- anorexia
- myalgias
- headache
- sore throat
- sore glands
- rash.

**Sign:**

- encephalopathy
- sepsis
- regally
- acute pharyngitis
- genital herpetiform ulceration
- skin rash (maculopapular or urticarial)
- viral meningitis
- Guillian-Barre syndrome
- *Pneumocystis pneumonia*†
- cryptococcal meningitis†
- oral/oesophageal candidiasis.

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

Severity of the syndrome ranges from mild non-specific 'viral' symptoms to a severe infectious mononucleosis-like illness with dysregulation and transient profound CD4 depletion.<sup>47,48</sup>

**Symptom:**

- malaise
- anorexia
- myalgias
- headache
- sore throat
- sore glands
- rash.

**Sign:**

- fever
- lymphadenopathy
- splenomegaly
- acute pharyngitis
- oral herpetiform ulceration
- maculopapular rash (maculopapular or urticarial)



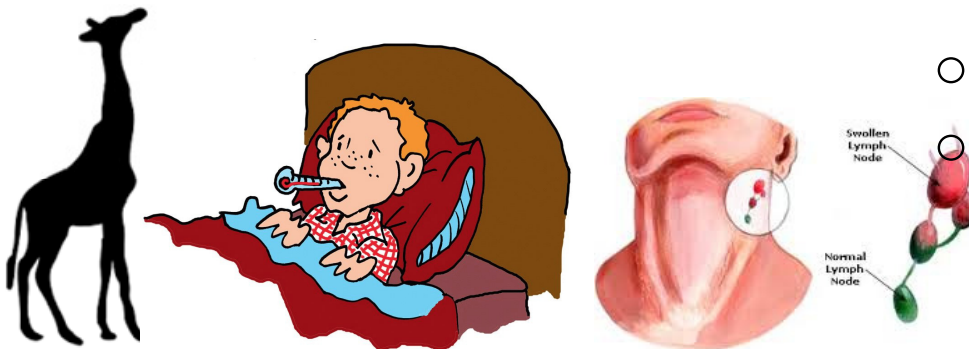
# Common symptoms and signs of acute HIV infection

## Symptom

- malaise
- anorexia
- myalgia
- headache
- sore throat
- sore glands
- rash

## Sign

- fever, sweating
- generalised lymphadenopathy
- hepatosplenomegaly
- non-exudative pharyngitis
- orogenital herpetiform ulceration
- truncal rash (maculopapular or urticarial)
- viral meningitis
- Guillian-Barre syndrome



# And the gifts keep coming

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

Severity of the syndrome ranges from mild non-spe

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

## General factors to consider:

- accessibility of condoms and compatible water-based lubri addressed
- no single HIV risk reduction intervention is likely to su
- combinations of prevention options, tailored to a be offered ('menu of prevention choices'), includ social/behaviour change interventions
- prevention options are likely to inc times available.

## Biomedical:

- male or female cond
- access to frequ
- early acc
- post-e
- p
- circumcision
- treatment
- exchange and opioid substitution therapy for people who inject

## 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.

**HIV PREVENTION METHODS**



# 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

