



SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

PrEP application in the SA Context

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AWACC

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USAID
FROM THE AMERICAN PEOPLE



health

Department:
Health
PROVINCE OF KWAZULU-NATAL

MatCH

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ANOVA
HEALTH INSTITUTE



WE



Definition: Key Populations

- **Key populations** are:

Men who have sex with men
Prison populations
People who inject drugs
Sex workers

Key populations are recognised **internationally**.

- **Vulnerable populations** are:

Adolescents and young women
Scholars
Immigrants
Others



Creating the Right Environment

- Make ***all patients*** feel equally welcome
(Not a “gay-identified” [VP and KP] space)
- Privacy for consultation
(Concern about disclosures of sexuality and status)
- Use patient’s name, gender pronouns (TG)
(Use their terms, not ours... Ask if/when not sure!)
- Posters addressing diverse sexual health needs of men
(No breastfeeding posters)
- Monitor your own response AND *the colleagues you supervise*





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

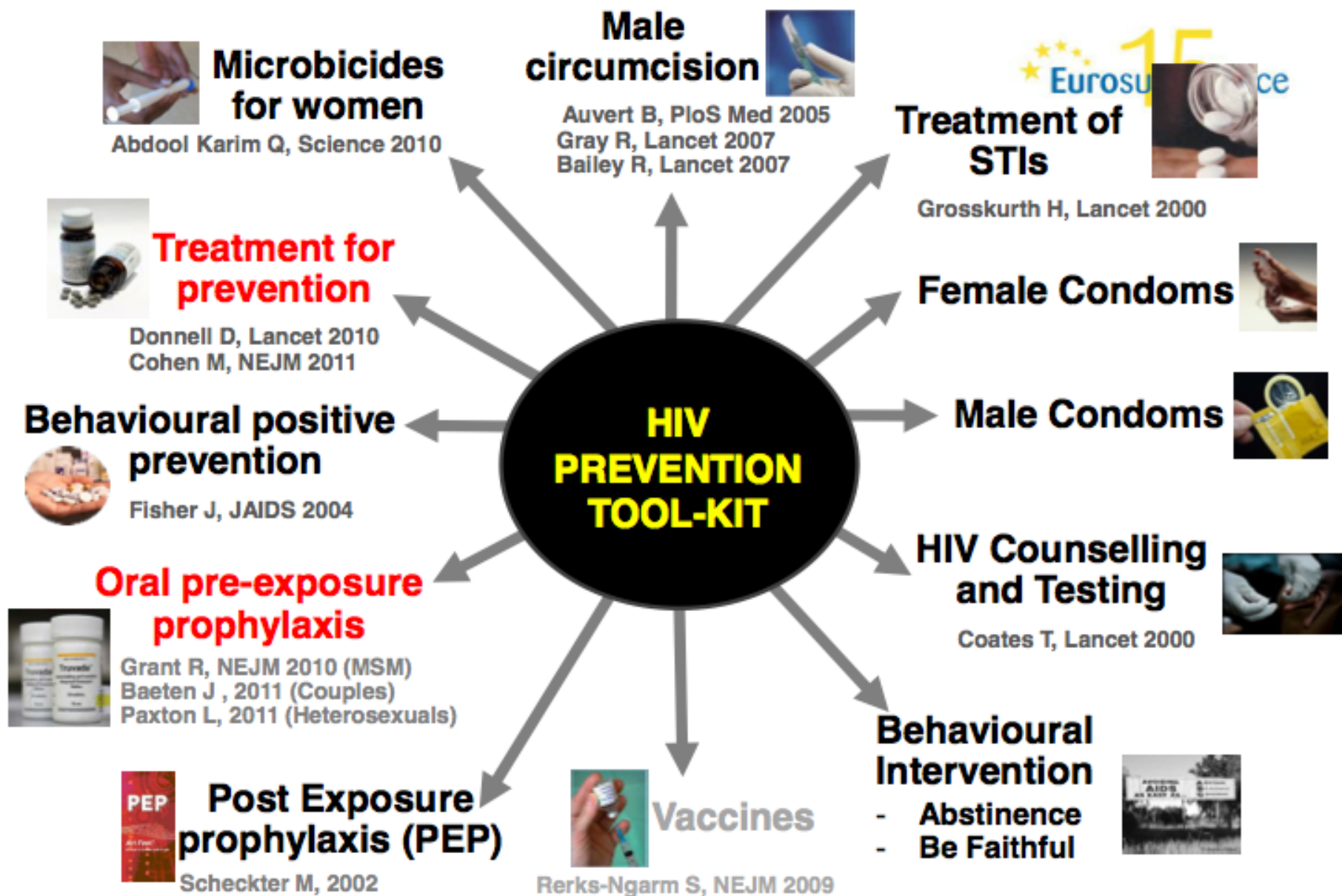
GUIDANCE ON PRE-EXPOSURE ORAL
FOR SERODISCORDANT COUPLES
WOMEN WHO HAVE SEX WITH
Recommendations for use in the
July 2012

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

GENERAL VIRAL THERAPY AND PRE-EXPOSURE PROPHYLAXIS FOR HIV

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014



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

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



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



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...

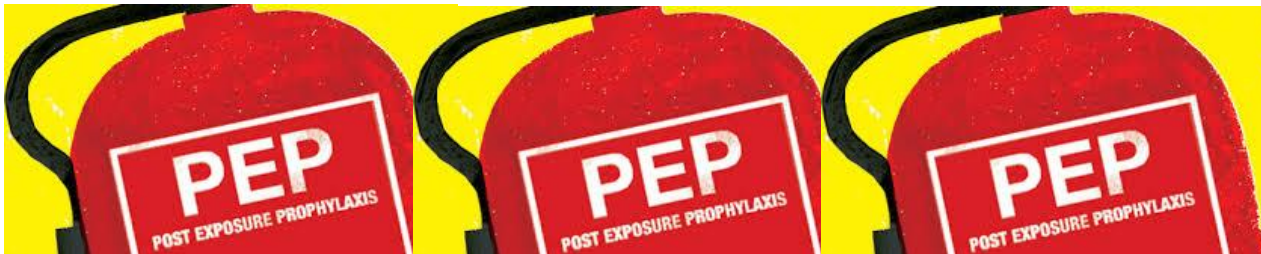
In the past six months:

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?



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



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



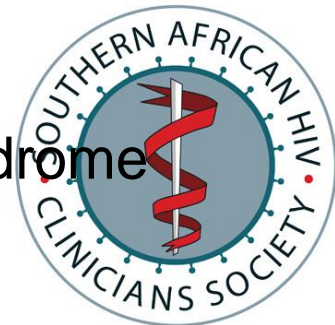
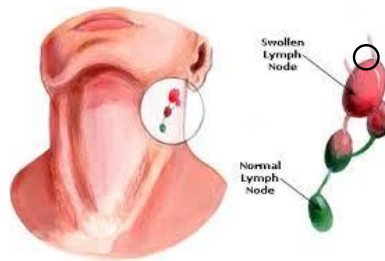
Common symptoms and signs of acute HIV infection

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



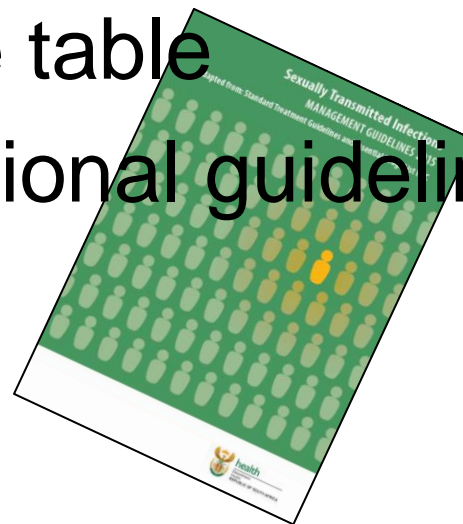
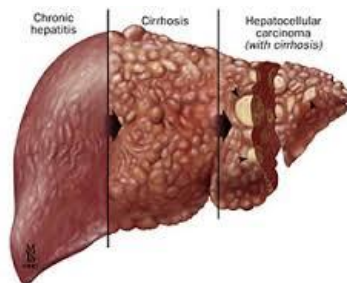
Starting PrEP

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.

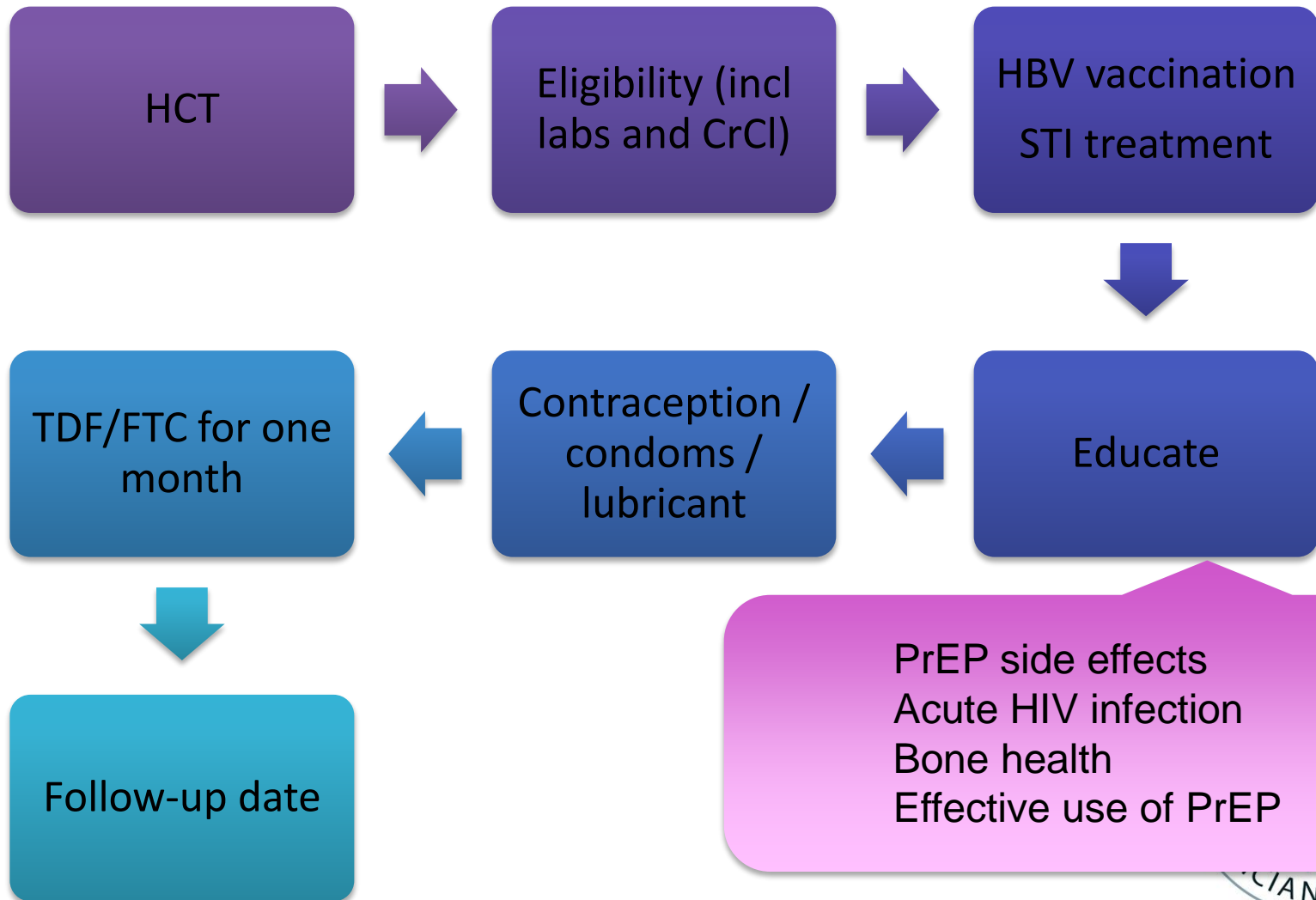
Hepatitis B surface antigen (HBsAg)	Hepatitis B surface antibody (HBsAb)	Action
Negative (-)	Negative (-)	Start PrEP, vaccinate concurrently
Negative (-)	Positive (+)	Start PrEP, no vaccine needed
Positive (+)	N/A	Refer for evaluation

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

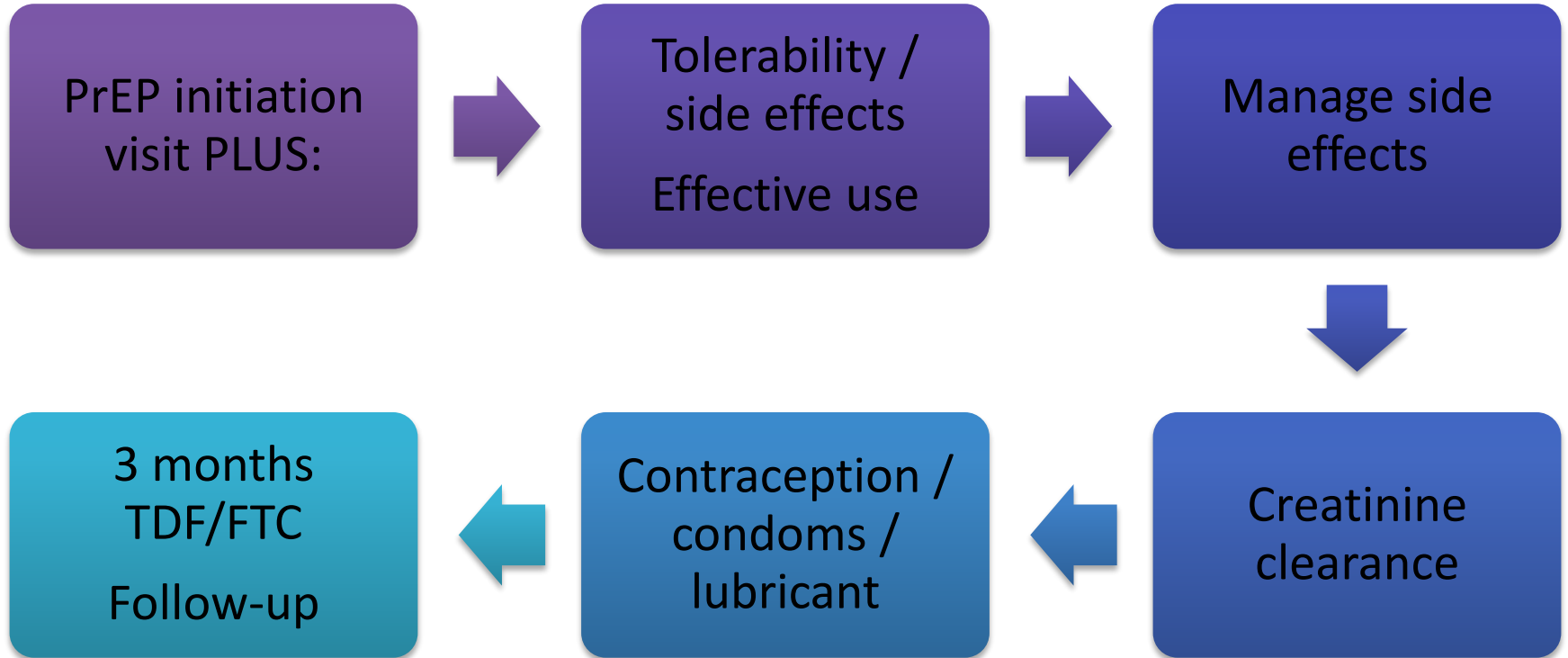
- Acute/chronic HBV: LFT monitoring



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

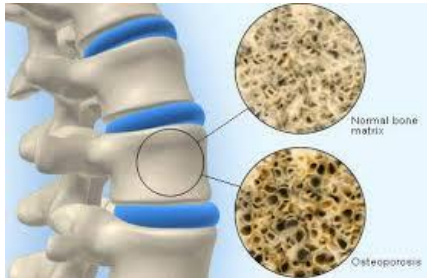


Risks and side effects



**ARV
resistance**

**HBV
management**



**Risk
compensation**



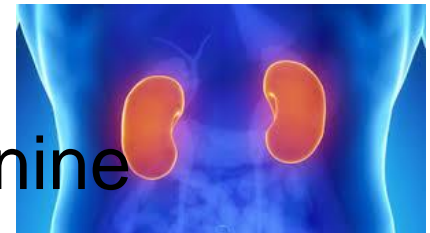
Resistance

- 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



Cycling On or Off PrEP

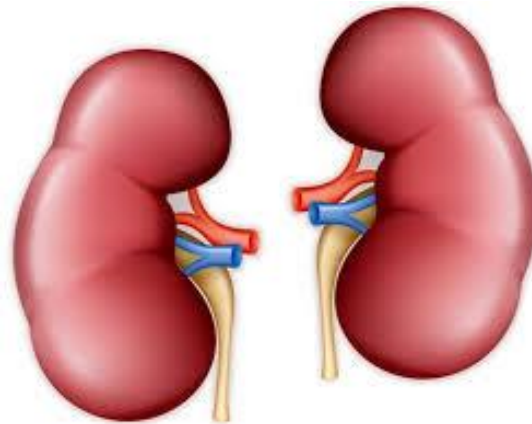


- PrEP is not a lifelong drug-taking intervention
- PrEP should be used only if there is possible exposure to HIV
 - Risk levels expected to change
 - People will use PrEP for variety of reasons
 - Case example e.g. student / CSW
- People can cycle off PrEP
- This is NOT non-adherence
- Remember lead in and lead out times



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



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



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
- no evidence adverse outcomes in infants exposed to TDF/FTC ART



In SA: TDF/FTC PrEP CI in pregnant or breastfeeding women





SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

PrEP Case Studies



Discordant Couple: Case Study 1

- 22 year old woman attends your CHC
- Previously well, no medical history of note
- Recently married
- Her husband is HIV positive and has been honest about his status
- Husband's CD4 count is 1000 cells/mm³
- She has been using condoms but her husband is not happy to continue using them



Discordant Couple: Case Study

What HIV prevention strategies are applicable to this couple?

– Condoms and lube



– PEP



– PrEP



– TasP / UTT



Discordant Couple: Follow Up

- Husband

- Advise treatment and link to care at nearest state ART facility
- Promote condom use
- Discussion that he should wait until he is virally suppressed before planning a family

- Wife comes to see you one month later

- Husband has not yet attended for ART
- Requests PrEP



Discordant Couple: Case Study



- Does she need PrEP?

Yes!

Ongoing exposure risk – husband not keen on condoms and she may not have the ability to negotiate consistent condom use

- Confirmation of HIV-negative status?

HIV fourth generation negative previously and on this visit

- What other baseline investigations are required?

Creatinine and creatinine clearance (>60 mL/min)

Hepatitis B surface antigen and antibody

STI screen

Pregnancy test! Advise contraception

All results are favourable

Start PrEP

Advise contraception

Discordant Couple: Case Study

- All well at months 1, 3 and 6
- Correct pill-taking
- Using condoms about 50% of the time
- Reports using oral contraceptive
- Husband started ART 4 weeks previously



USS scan confirms
viable 20 week
male foetus



- What do you do now?
- Do you stop PrEP?



	Stop PrEP	Continue PrEP
Mother	Ongoing HIV risk to mom (5% incidence in some studies)	Protects mom
Baby	Minimises risk to baby	Risk of bone abnormalities but insufficient data

MCC contra-indicates Truvada use for PrEP during pregnancy

Tenofovir is FDA category B risk in pregnancy

Lots of experience of use in pregnant HIV-positive mothers

Case by case decision based on risks and benefits



Discordant Couple: Outcome



- Elected to stop PrEP
 - Couple were prepared to use condoms consistently as long as not permanent
-
- Successful normal delivery
 - Baby (and mom) remain HIV-negative
 - Husband now on ART and VL LDL



Case 2



- 62 year old single gay man
- First contact with clinic in Nov 2011
 - Unprotected sex 60 hours previously
 - Received PEP
 - Remained HIV-negative
- Repeat exposures requiring PEP in 2013, 2014 and 2015
- Primary sex partner is HIV-positive on ART
- Enquired about PrEP in July 2015



Case 2

- Does he need PrEP?

Yes!

Ongoing exposure risk – not using condoms constantly

- Confirmation of HIV-negative status?

HIV fourth generation negative previously and on this visit

Sexual history – last possible exposure 10 days ago

Clinical assessment – current URTI (presumed viral)

- What other baseline investigations are required?

Creatinine and creatinine clearance (>60 mL/min)

Hepatitis B surface antigen and antibody

STI screen



Case 2: Results

- HIV rapid test negative
- Creatinine 98 $\mu\text{mol/L}$
- MDRD GFR >60 mL/min
- HBsAg-negative
- HBsAb-positive
- Do you start PrEP?



Delay PrEP and review in 2-4 weeks
Counselling / condoms / lubricant
2 Week visit: HIV-negative and clinically well
Start PrEP



Case 2: 1 Month Follow Up

- Correct pill-taking confirmed
- No current STIs
- Ongoing potential HIV exposures
- Side effects settled after 5 days
- What tests are required?

Confirmation of HIV-negative status
STI screening?
Repeat creatinine and creatinine clearance

Creatinine

117

Cr Cl 56

Case 2: Ongoing management

Stop PrEP

- Client is a doctor!
 - Counselling about risks and benefits
 - Ongoing high risk of HIV exposure
 - Unwilling to increase condom use
 - Social event with excess alcohol the day before monitoring occurred
- Chooses not to stop but to increase monitoring



Case 2: Ongoing management

Search for alternative causes of renal dysfunction

- Not hypertensive
- Normal random glucose
- Total fasted cholesterol 5.3
- No nephrotoxic agents (e.g. no NSAIDs)
- No family history
- Normal urine dipstix (no proteinuria)

Repeat Renal Function:
Creatinine 103
Cr Cl >60

Case 2: 3 Month Follow Up

- Correct pill taking confirmed
- No current STIs
- Repeat creatinine
- Scripted 3 months of PrEP
- Stop PrEP
- Counselling/advice about HIV prevention

Creatinine

135

Cr Cl 48



Case 2: Outcome



- Patient does not want to stop PrEP
- Elected to continue despite medical advice with close monitoring
- Renal function has improved slightly and stabilised (Cr Cl approx 55)
- Increasing comfort level that tenofovir-induced renal dysfunction may plateau
- **AGAINST** current guidelines!



TAKING A SEXUAL HISTORY: MSM

START BY:

HAVE YOU HAD SEX WITH ANYONE IN THE LAST 6 MONTHS?

NO

Explore reasons why not sexually active

ASK ABOUT:

- Stress, depression and mental health concerns
- Relationship problems
- Physical problems such as warts or hemorrhoids that may be causing psychological embarrassment
- Sexual dysfunction
- Anxiety related to HIV infection



YES

Within the last 6 months, have you had sex with...

MEN

BOTH

WOMEN

Consider as MSM and explore further

When you have sex with men...

... have you ever had ORAL sex?

YES

NO

During ORAL sex, were you...

RECEPTIVE

BOTH

INSERTIVE

Consider possible PHARYNGEAL STI

Consider possible PENILE/GENITAL STI

ASK ABOUT: pain, difficulty swallowing, sores and ulcers
PERFORM: oral examination

ASK ABOUT: pain, discharge, burning on urination, sores, ulcers, growths
PERFORM: penile and scrotal examination

... have you ever had ANAL sex?

YES

NO

During ANAL sex, were you...

RECEPTIVE

BOTH

INSERTIVE

Consider possible ANAL STI

Consider possible PENILE/GENITAL STI

ASK ABOUT: pain, discharge, sores, ulcers, bowel habit and tenesmus
PERFORM: anal examination

ASK ABOUT: pain, discharge, burning on urination, sores, ulcers, growths
PERFORM: penile and scrotal examination



Condom use » If not, explore reasons and discuss how to improve condom use
Lubrication » If not water-based, explore reasons why not and educate

Sexually Transmitted Infections

- Have you previously been diagnosed with any STIs and what were the symptoms?
- What treatment did you receive?
- Did you complete the treatment course?
- Was your partner notified, screened and/or treated?

Case 3: Jackie

- Jackie is 15 and lives in an area where gangs and crime are rife.
- She has been raped once, so have many of her friends.
- Her mother brings her in the clinic to discuss the prevention against HIV and pregnancy.
- She also suspects her daughter and her boyfriend are having sex, although Jackie denies it.
- Her mother has heard about this PrEP pill and thinks this should be given to her daughter.



Case 3: Jackie

- What is your personal feeling about this? How would you handle this professionally?
- Is Jackie eligible for PrEP?
- What additional information do we need to confirm eligibility ?
- What are her rights? what are her mother's right to protect her?
- What issues would you discuss with them?

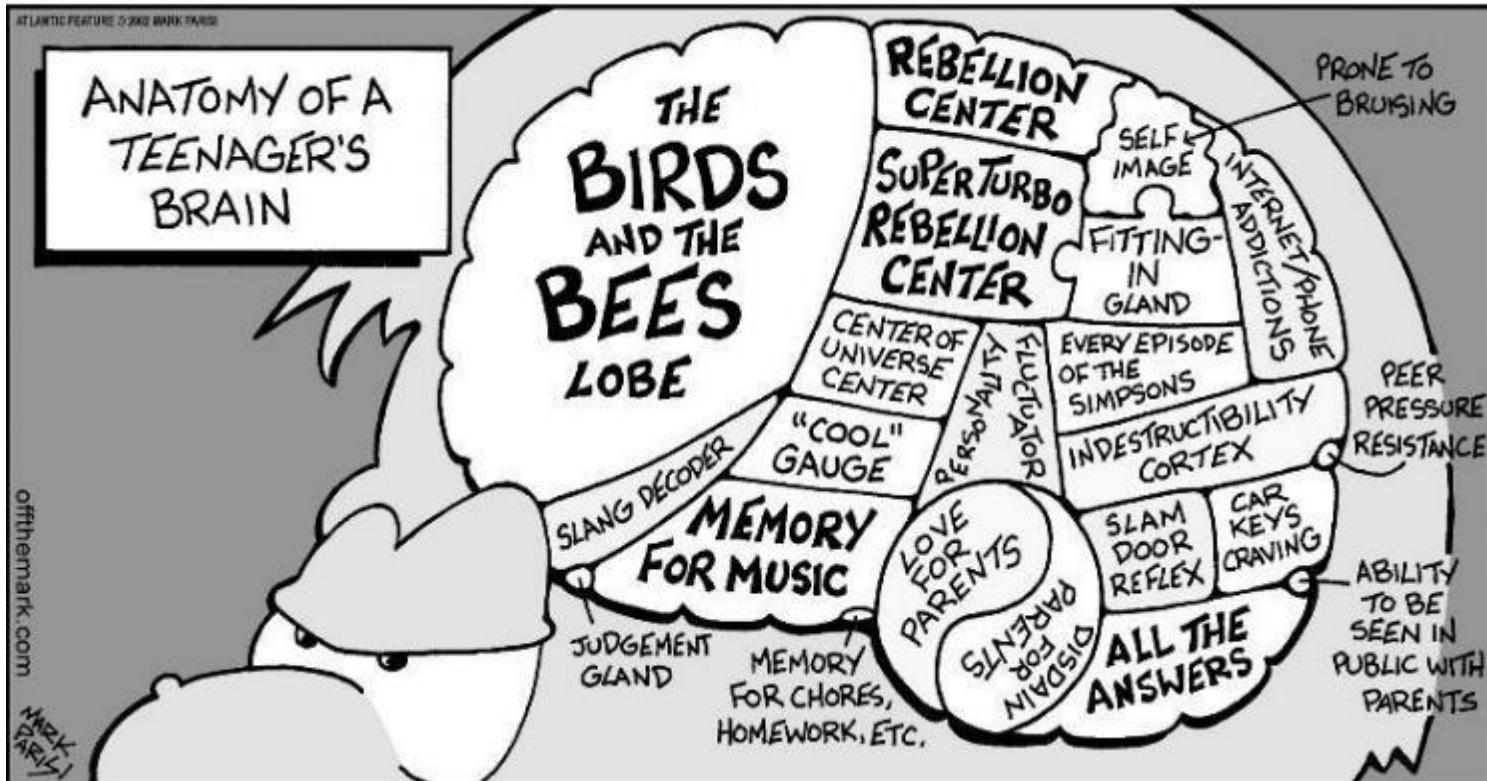


PreP in Adolescents

Adolescent Brain

off the mark.com

by Mark Parisi



Major challenges for Adolescents

- Living with HIV
- Stigma
- Disclosure vs. non-disclosure
- Adherence
- Reproductive health and sexuality
- Mental health
- Transition to adulthood



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

