HIV PREVENTION

SAMU SUMMARY

2018
Objectives

- To describe the current situation regarding new HIV infections globally
- To list the global HIV prevention targets
- To list all types of HIV prevention strategies and know their relative effectiveness
- To describe the landmark studies for different prevention strategies
- To be able to assess HIV acquisition risk
Percent change in new HIV infections among adults (aged 15 years and older), from 2005 to 2015

The risk of HIV acquisition compared to adults (aged 15 years and older) in the general population:

- Sex workers: 10 TIMES
- People who inject drugs: 24 TIMES
- Gay men and other men who have sex with men: 24 TIMES
HIV incidence in women aged 18-35 years in this community:

9.1 per 100 women-years (95% CI: 7 - 12)

Source: Abdool Karim Q et al, Science 2010

HIV in pregnant women in rural South Africa (2001-2013)

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<tr>
<th>Age Group (Years)</th>
<th>HIV Prevalence (N=4818)</th>
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<tr>
<td>&gt;25</td>
<td>51.9%</td>
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Source: Abdool Karim Q, Int J Epi, 2014
Who are the people with potential for transmission?
VL > 1000 cp/ml, Eshowe, KZN, SA 2016

People w VL> 1000 by risk behaviour, gender and age

Source: KZN survey 2013
REDUCTIONS IN NEW INFECTIONS ARE OFF TARGET

NEW HIV INFECTIONS, ALL AGES, GLOBAL, 1990–2016 AND 2020 TARGET

Source: UNAIDS 2017 estimates.

*The 2020 target is fewer than 500,000 new HIV infections, equivalent to a 75% reduction since 2010.
New adult HIV infections declined by less than 10% between 2010 and 2014: 50% reduction target missed.
What changed our perspectives on prevention
‘We today have the science to turn this epidemic down. Political commitment will decide’ T. Fauci, head of NIAID
Treatment as Prevention (TasP)  
HPTN 052 -> intervention on the HIV(+) partner

Treatment of sero-discordant couples (n=1783)  
(Malawi, Zimbabwe, Botswana, Kenya, South Africa, Brazil, Thailand, the US and India)

HIV pos partner  
treatment up to 550 CD4

No treatment for HIV pos partner above 250 CD4

1 genetically linked infection (during the early months of treatment)

27 genetically linked infection

Treatment reduced the risk of HIV transmission to an uninfected partner – by at least 96%

Morbidity and mortality: 40 vs 60 cases (EPTB: 3 vs 17 cases)

Courtesy: Veronica Miller, Forum for Collaborative HIV Research
The PARTNER study recruited HIV serodiscordant couples (one partner positive, one negative) at 75 clinical sites in 14 European countries.

They tested the HIV-negative partners every six to 12 months for HIV, and tested viral load in the HIV-positive partners.

In cases of HIV infection in the negative partners, their HIV was genetically analysed to see if it came from their regular partner.

The study found no transmissions between gay couples where the HIV-positive partner had a viral load under 200 copies/ml – even though there were nearly 77,000 acts of condomless sex between them.

The results indicate, in the words of the researchers, “A precise rate of within-couple transmission of zero” for gay men as well as for heterosexuals.
U=U

UNDetectable = UNtransmittable

A person living with HIV who has an undetectable viral load does not transmit the virus to their partners.
UNAIDS Prevention targets and pillars

Pillars for achieving less than 500,000 new infections by 2020

1. Combination prevention for adolescent girls and young women
2. Combination prevention with key populations
3. Comprehensive condom programmes
4. Voluntary medical male circumcision and sexual and reproductive health services for men and boys
5. Rapid introduction of pre-exposure prophylaxis
How many ways can you do it?

List all the ways you know how to prevent HIV transmission

Once you have listed them put them in the order from least effective to most effective
STRUCTURAL INTERVENTIONS
Girls and young women ages 13–22 who received regular small cash payments were less than half as likely to acquire HIV.

Girls who received payments were 75 percent less likely to acquire herpes simplex virus 2 (HSV-2).

were also more likely to attend school, less likely to have sex regularly and a partner older than 25 years.
National sex work policy and HIV prevalence among sex workers: an ecological regression analysis of 27 European countries

• Countries that have legalised some aspects of sex work (n=17) have significantly lower HIV prevalence among sex workers than countries that criminalise all aspects of sex work
BIOMEDICAL INTERVENTIONS
Number of HIV infections averted through condom use, global, 1990–2015


45 million infections have been averted by condom scale-up.
Role of Circumcision
Scientific Evidence: Male Circumcision Reduces HIV Risk

- Lack of male circumcision/higher HIV prevalence
- Randomised controlled trials in Kenya, Uganda, and South Africa stopped early: **60% protection**
- Protective effect sustained/increased
Figure 1. Annual* number of voluntary medical male circumcisions performed for HIV prevention in 14 countries in East and Southern Africa, 2008–2017

Cumulative total: 18,581,880 through 2017

*Calendar year.

Source: Global AIDS Response Progress Reporting from national programmes, UNAIDS/UNICEF/WHO.
NON-SURGICAL TECHNIQUES FOR CIRCUMCISION
WHAT IS THE MEDICAL MALE CIRCUMCISION PROCESS?

1. You will be approached by the MSF mobilisation team or a health professional. The MSF mobilisation team or a Department of Health staff will approach you and explain the benefits and limitations of male medical circumcision to you. You will be asked to consent to an HIV test and the male medical circumcision procedure. If you are under 18 years of age, your consent has to be approved by a parent or guardian. You will be given an appointment for your circumcision, and in some cases a time and place close to your home from where you will be picked-up and transported for free to the health facility.

2. You will receive counselling and HIV testing before undergoing circumcision. When you arrive at the clinic or hospital, you will receive group counselling and you can voluntarily test for HIV before undergoing circumcision. You will also be examined for sexually transmitted infections and foreskin abnormalities.

3. Your circumcision will be performed by a trained health professional; it's painless and quick. The circumcision will be done by a doctor or nurse specially trained to perform this kind of procedure. It is done under local anaesthetic, so besides a small injection, there is no pain and it takes only about 30 minutes.

The wound is then stitched and dressed, and you are given painkillers to help manage any mild pain or discomfort you may have when the anaesthetic wears off. You are also given instructions on how to keep the wound clean while it heals, as well as a medical certificate should you require time off from work or studies while you recover.

4. You can go back home the same day. Most times you will not need to stay overnight in the hospital. You can go home, or in some cases may be taken home by the MSF team.

5. You will heal completely in 6 weeks. The healing process takes six weeks, during which time you may not have sex or masturbate. If you do, the wound will take longer to heal completely — and you run a higher risk of HIV transmission.

For the first few days, you must keep the bandage on and keep it dry. In 7 days you will return to the health centre for a follow-up visit and to have the bandage removed. After this, you should wash your penis with salt and water, using a soft cloth. The stitches will fall out after 10 to 14 days. In 6 weeks you will have a final check-up.

If you have more questions, speak to us:
MSF: 035 4741002 or 072 3402089
Hospital/Clinic: ........................................... 

Your Circumcision Appointment 

Site: ..............................................................
Date: ..... / ..... / ...... Day: .........................
Time: ........... : ...........
Pick-up place: ............................................
Pick-up time: ........... : ...........
Responsible / contact: .....................................

Make the right choice!
GET CIRCUMCISED

- Reduced risk of HIV
- Reduced risk of STIs
- Improved hygiene
TASP
Progress toward the 90–90–90 target, by region, 2015

Source: UNAIDS special analysis, 2016; for more details, see annex on methods.
## Does TASP work in real life?
### HIV incidence – 3 countries-Epicentre survey

<table>
<thead>
<tr>
<th>Country</th>
<th>Malawi %</th>
<th>South Africa %</th>
<th>Kenya %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current guidelines</td>
<td>80.4</td>
<td>75.0</td>
<td>70.8</td>
</tr>
<tr>
<td>New guidelines</td>
<td>73.5</td>
<td>64.3</td>
<td>51.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Malawi %</th>
<th>South Africa %</th>
<th>Kenya %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>-</td>
<td>1.6</td>
<td>2.8</td>
</tr>
<tr>
<td>Men</td>
<td>-</td>
<td>0.6</td>
<td>1.3</td>
</tr>
<tr>
<td>Overall</td>
<td>0.4</td>
<td>1.2</td>
<td>2.2</td>
</tr>
</tbody>
</table>

PY: person-years
Caprisa, Voice, FACTS 001 – topical gels did not provide protection (mainly due to low adherence)

Vaginal ring studies (ASPIRE, Ring Trial) showed moderate protection (30% overall), and 60% for those with high levels of adherence, but...

The ring was completely ineffective among women under age 21. Low adherence? Biology/physiology?
MTN-020/ASPIRE & IPM-027: Dapivirine Vaginal Ring for HIV Prevention in Women

- Silicone elastomer vaginal matrix ring containing NNRTI dapivirine 25 mg; ring replaced every 4 wks
- Randomized, double-blind phase III trials
  - MTN-020/ASPIRE\(^1,2\): Malawi, South Africa, Uganda, Zimbabwe
  - IPM-027 (The Ring Study)\(^3\): South Africa, Uganda
  - Primary endpoints: efficacy and safety

Sexually active HIV-uninfected adult women

- ASPIRE: N = 2629;
- IPM-027: N = 1959

Dapivirine 25 mg Vaginal Ring every 4 wks
+ HIV Prevention Service Package
  (ASPIRE: n = 1313; IPM-027: n = 1300)

Placebo Vaginal Ring every 4 wks
+ HIV Prevention Service Package
  (ASPIRE: n = 1316; IPM-027: n = 650)

MTN-020/ASPIRE & IPM-027: Efficacy and Safety of Dapivirine Vaginal Ring

- Efficacy for HIV prevention similar in both studies
- No clinically relevant safety differences between arms

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ASPIRE(^{[1,2]}): 15 Sites</th>
<th>ASPIRE(^{[1,2]}): 13 Sites*</th>
<th>The Ring Study(^{[3]})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dapivirine (n = 1308)</td>
<td>Dapivirine (n = 1198)</td>
<td>Dapivirine (n = 1300)</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 1306)</td>
<td>Placebo (n = 1197)</td>
<td>Placebo (n = 650)</td>
</tr>
<tr>
<td>HIV infections, n</td>
<td>71</td>
<td>54</td>
<td>77</td>
</tr>
<tr>
<td>HIV incidence (per 100 PYs)</td>
<td>3.3</td>
<td>2.8</td>
<td>4.1</td>
</tr>
<tr>
<td>HIV protection efficacy, %</td>
<td>27 ((P = .046))</td>
<td>37 ((P = .007))</td>
<td>31 ((P = .040))</td>
</tr>
<tr>
<td>Among women older than 21 yrs</td>
<td>-</td>
<td>56 ((P &lt; .001))</td>
<td>37 ((P = .10))</td>
</tr>
</tbody>
</table>

Excludes 2 sites with low adherence.

Oral pre-exposure prophylaxis (PrEP) for populations at substantial HIV risk: Universal Test and Treat?
Daily TDF/FTC and 3 monthly HIV test
For the first time in my life, oral Prep allows me to own my sexuality

Sinazo Peters 22 yrs,
Former “Future Fighter”
Desmond Tutu HIV Foundation
Clinical Trial Evidence for HIV Prevention Options (February 2016)

### Prevention of sexual transmission

<table>
<thead>
<tr>
<th>Study/Intervention</th>
<th>Effectiveness (%)</th>
<th>Effect size (CI)</th>
</tr>
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<tr>
<td>PROUD – daily oral TDF/FTC (MSM – United Kingdom)</td>
<td>86%</td>
<td>86% (58; 97)</td>
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<tr>
<td>IPERGAY – event-driven TDF/FTC (MSM – Canada, France)</td>
<td>86%</td>
<td>86% (44; 99)</td>
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<tr>
<td>Partners PrEP – daily oral TDF/FTC (Serodiscordant couples – Kenya, Uganda)</td>
<td>75%</td>
<td>75% (55; 87)</td>
</tr>
<tr>
<td>Partners PrEP – daily oral TDF (Serodiscordant couples – Kenya, Uganda)</td>
<td>67%</td>
<td>67% (44; 81)</td>
</tr>
<tr>
<td>TDF2 – daily TDF/FTC (Heterosexual men and women – Botswana)</td>
<td>62%</td>
<td>62% (22; 84)</td>
</tr>
<tr>
<td>iPrEx – daily oral TDF/FTC (MSM – North and South America, South Africa, Thailand)</td>
<td>44%</td>
<td>44% (15; 63)</td>
</tr>
<tr>
<td>CAPRISA 004 – BAT-24 dosing vaginal tenofovir gel (Women – South Africa)</td>
<td>39%</td>
<td>39% (6; 60)</td>
</tr>
<tr>
<td>RV 144 – six injectable ALVAC/AIDSVAX (Heterosexual men and women – Thailand)</td>
<td>31%</td>
<td>31% (1; 51)</td>
</tr>
<tr>
<td>The Ring Study – monthly vaginal ring containing dapivirine (Women – South Africa, Uganda)</td>
<td>27%</td>
<td>27% (1; 46)</td>
</tr>
<tr>
<td>ASPIRE – monthly vaginal ring containing dapivirine (Women – Malawi, South Africa, Uganda, Zimbabwe)</td>
<td>15%</td>
<td>15% (-21; 40)</td>
</tr>
<tr>
<td>MTN 003/VOICE – daily dosing vaginal tenofovir gel (Women – South Africa, Uganda, Zimbabwe)</td>
<td>6%</td>
<td>6% (-21; 40)</td>
</tr>
<tr>
<td>FEM-PreP – daily oral TDF/FTC (Women – Kenya, South Africa, Tanzania)</td>
<td>0%</td>
<td>0% (-40; 30)</td>
</tr>
<tr>
<td>FACTS 001 – event-driven vaginal tenofovir gel (Women – South Africa)</td>
<td>-4%</td>
<td>-4% (-49; 27)</td>
</tr>
<tr>
<td>MTN 003/VOICE – daily oral TDF (Women – South Africa, Uganda, Zimbabwe)</td>
<td>-49%</td>
<td>-49% (-129; 3)</td>
</tr>
<tr>
<td>MTN 003/VOICE – daily oral TDF (Women – South Africa, Uganda, Zimbabwe)</td>
<td>49%</td>
<td>49% (10; 72)</td>
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### Prevention in people who inject drugs

<table>
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<th>Study/Intervention</th>
<th>Effectiveness (%)</th>
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<tr>
<td>Bangkok Tenofovir Study – daily oral TDF (PWID – Thailand)</td>
<td>49%</td>
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**DELIVERY SYSTEM**
- Vaccine
- Oral pills
- Vaginal gel
- Vaginal ring

**ACTIVE DRUG**
- Tenofovir
dapivirine
- Tenofovir disoproxil fumarate (TDF)
- Emtricitabine (FTC)
- ALVAC/AIDSVAX
The findings of the PrEP trials in all populations have been strikingly consistent: in individuals who took the drug as prescribed (as determined by levels of drug detectable in the blood), there was high levels of protection. Adherence and protection are closely linked in all participants and subgroup analyses across all of the trials to date. The overall efficacy findings reported by various trials reflect analyses of all participants; most trials have also provided subgroup analyses focusing on protection in those who had detectable drug in the blood. The two sets of findings – overall and adherence-related – have sometimes been used interchangeably and may cause confusion, as two trials of daily oral tenofovir-based PrEP in young women found no efficacy, but also found very low adherence. This is consistent with the findings of other trials—eg that PrEP works when taken, but has led to confusion as to whether PrEP works for women.
What About Sexual Risk-Taking?
Data from Clinical Trials

- In both iPrEx and Partners PrEP, condomless sex became less common over time.
- BUT subjects did not know if they were on PrEP or placebo.

iPrEx

![Graph showing percent reporting URAI over weeks since randomization.]

Partners PrEP

![Graph showing proportion of HIV participants with any unprotected sex over follow-up time (month).]

Follow-up time (Month)

- TDF
- FTC/TDF
- Placebo
Who should receive PREP?

• All those at substantial risk
  – Above 3% per year
• Additional prevention choice
• In a comprehensive package
Example of PreP Assessment Tools from Zimbabwe

**Indications for PrEP**
- In Zimbabwe, groups that are likely to be at substantial risk (>3% incidence) of HIV infection include:
  - Adolescent girls and young women
  - Male and female sex workers
  - At-risk men (MSM, prisoners, truck drivers)
  - Sero-discordant couples
  - Women in relationships with men of unknown status
  - Transgender people

**Contraindications for PrEP**
- HIV-positive status
- Unknown HIV status
- Allergy to any medicine in the PrEP regimen
- Unwilling/unable to adhere to daily PrEP regimen
- Known renal impairment: estimated creatinine clearance <60ml/min

**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:
  - 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 post-exposure prophylaxis (PEP), OR
  - Requesting PrEP

**Practical screening questions for PrEP**
- Any “yes” answer should prompt a discussion of the risks and benefits of PrEP

**PrEP in sero-discordant couples**
- Any “no” answer to any of the questions below, may indicate increased risk for HIV infection and indication for PrEP

- Is your HIV positive partner taking antiretroviral therapy (ART) for HIV?
- Has your partner been on ART for more than 6 months?
- At least once a month, do you discuss whether your partner is taking therapy daily?
- If you know when your partner had his or her last HIV viral load test, what was the result?
- Do you use condoms every time you have sex?
- Are you using effective contraception with a HIV-positive partner?
Tete:
Overall 60% HIV positive
38% of negative re-test within 6 months and 8 (4%) seroconverted

Sofala:
Overall 55% HIV positive
49% of negative re-test within 6 months and 7 (10%) seroconverted
HIV in pregnant women in rural South Africa (2001-2013)

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HIV incidence in 18-35 year women in this community:

9.1% per 100 women-yrs (95% CI: 7 - 12)

Source: Abdool Karim Q et al, Science 2010
Should MSF provide PREP?

• Research?
• Routine implementation?
• Demonstration projects.....
Important questions to answer

• Who should receive PrEP?
  – Risk? Motivation?

• In what health care setting?
  – STI, FP, ANC, HIV, Community

• How?
  – Health promotion? Adherence support?
  – Clubs CAGs etc

• What monitoring needed?

• Risk/benefit in:
  – Pregnant and breast-feeding women?
  – Renal/bone risk groups
  – Non-adherent people

• Use of 3TC instead of FTC?
PREP to promote testing and linkage:
Self-testing could simplify access and reduce costs
Long acting PREP?

Rilpivirine (TMC 282) and GSK744 LAP in pipeline

Mean Plasma GSK1265744 Concentration-Time Profiles following Single Dose LAP Injections in Healthy Subjects
We need options....

PrEP in the future

- Pill
- Gel
- Vaginal film
- Vaginal ring
- Injectable
## Existing and potential future prevention interventions

<table>
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<tr>
<th>Intervention</th>
<th>Efficacy</th>
<th>Available</th>
<th>Priority risk group?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms</td>
<td>90%</td>
<td>Now</td>
<td>FSW</td>
</tr>
<tr>
<td>VMMC</td>
<td>60%</td>
<td>Now</td>
<td>Young men</td>
</tr>
<tr>
<td>Early ART</td>
<td>85%</td>
<td>Now</td>
<td>All</td>
</tr>
<tr>
<td>Oral PrEP</td>
<td>90%</td>
<td>Now</td>
<td>FSW, high-risk young women</td>
</tr>
<tr>
<td>IVR</td>
<td>65%</td>
<td>2017</td>
<td>FSW</td>
</tr>
<tr>
<td>LA-ARVs</td>
<td>90%</td>
<td>2020</td>
<td>FSW, high-risk young women</td>
</tr>
<tr>
<td>BNAbs</td>
<td>90%</td>
<td>2028</td>
<td>FSW, high-risk young women</td>
</tr>
<tr>
<td>Imperfect vaccine</td>
<td>50%</td>
<td>2024</td>
<td>14 year-olds</td>
</tr>
<tr>
<td>Idealised vaccine</td>
<td>70%</td>
<td>2030</td>
<td>14 year-olds</td>
</tr>
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Clinical Trial Evidence for HIV Prevention Options (February 2016)

Prevention of sexual transmission

- PROUD – daily oral TDF/FTC (MSM – United Kingdom)
- IPERGAY – event-driven TDF/FTC (MSM – Canada, France)
- Partners PrEP – daily oral TDF/FTC (Serodiscordant couples – Kenya, Uganda)
- Partners PrEP – daily oral TDF (Serodiscordant couples – Kenya, Uganda)
- TDF2 – daily TDF/FTC (Heterosexual men and women – Botswana)
- iPrEx – daily oral TDF/FTC (MSM – North and South America, South Africa, Thailand)
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- RV 144 – six injectable ALVAC/AIDSVAX (Heterosexual men and women – Thailand)
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- FACTS 001 – event-driven vaginal tenofovir gel (Women – South Africa)
- MTN 003/VOICE – daily oral TDF (Women – South Africa, Uganda, Zimbabwe)
- Bangkok Tenofovir Study – daily oral TDF (PWID – Thailand)

Prevention in people who inject drugs

- Partners PrEP – daily oral TDF (Serodiscordant couples – Kenya, Uganda)

Effect size (CI)

86% (58; 97)
86% (44; 99)
75% (55; 87)
67% (44; 81)
62% (22; 84)
44% (15; 63)
39% (6; 60)
31% (1; 51)
27% (1; 46)
15% (-21; 40)
6% (-21; 40)
0% (-40; 30)
-4% (-49; 27)
-49% (-129; 3)
49% (10; 72)

Adapted from: Salim S. Abdool Karim, CAPRISA
PREVENTION GAPS

Only 38% of people living with HIV are virally suppressed.

Condoms available in sub-Saharan Africa cover less than half of the need.

Two-thirds of young people do not have correct and comprehensive knowledge of HIV.

Condom use is much too low across all population groups at higher risk of infection.

43% of countries with documented injecting drug use do not have needle-syringe programmes in place.

The annual number of voluntary medical male circumcisions must nearly double to reach the 2020 target.

PrEP coverage is less than 5% of the 2020 target.
Should MSF be more involved in prevention activities?
Prevention resources

- See the prevention resource section of samumsf.org