Biomedical Prevention interventions for Women

What do we know? - where do we go?

Linda-Gail Bekker
The Desmond Tutu HIV Centre, UCT, Cape Town, RSA.
March 2017
78 million people infected, 39 million people dead
37 million living with HIV today

2 million people became infected in 2014
An urgent and ongoing crisis:

2500 infections every day: 1 new infection every 30 seconds

80% of new infections in SSA
AVOIDING AIDS AS EASY AS...

ABSTAIN BE FAITHFUL

CONDOMISE
HIV in retreat....

- 15.8 million on ART June 2015
- New HIV infections down by 35% since 2000
- New infections among children down by 50% since 2000
- AIDS related deaths down by 42% since 2004
- TB related deaths down by 32% since 2004
HIV in SSA: the Epidemic Goes On

People living with HIV in sub-Saharan Africa, 2013

Source: UNAIDS 2013 estimates

UNAIDS Gap Report, 2014
## HIV in SSA AMP Countries

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Botswana</td>
<td>300 000</td>
<td>23.4</td>
<td>160 000</td>
<td>15 000</td>
<td>4 200</td>
</tr>
<tr>
<td>Kenya</td>
<td>1,600 000</td>
<td>6.2</td>
<td>800 000</td>
<td>220 000</td>
<td>62 000</td>
</tr>
<tr>
<td>Malawi</td>
<td>910 000</td>
<td>10.0</td>
<td>430 000</td>
<td>170 000</td>
<td>44 000</td>
</tr>
<tr>
<td>Mozambique</td>
<td>1,400 000</td>
<td>11.3</td>
<td>750 000</td>
<td>200 000</td>
<td>74 000</td>
</tr>
<tr>
<td>SA</td>
<td>5,600 000</td>
<td>17.3</td>
<td>2,900 000</td>
<td>460 000</td>
<td>270 000</td>
</tr>
<tr>
<td>Tanzania</td>
<td>1,800 000</td>
<td>5.6</td>
<td>760 000</td>
<td>230 000</td>
<td>84 000</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>1,200 000</td>
<td>14.9</td>
<td>600 000</td>
<td>200 000</td>
<td>58 000</td>
</tr>
</tbody>
</table>
New HIV Infections in Adolescents (15-19) in 20 Countries with Highest Number of New HIV Infections, 2012

Source: UNAIDS 2012 HIV and AIDS estimates
HIV in SSA: the Epidemic Among Women

In 2013, of the 24.7 million people HIV infected in SSA >50% were women
Young women are twice as likely to be infected as young men
Women have fewer HIV prevention options than men

Source: UNAIDS 2013 estimates
UNAIDS Gap Report, 2014
6.4 million live with HIV (12.2%)
Women 30-34 years – prevalence 36%
Men 35-39 years – prevalence 29%
>3 million South Africans on ART
400 000 new HIV infections in 2012
Young women and girls.

Women: 15-24 years 4 x higher than male peers
Girls: 10-19 years 8 x higher than male peers
Highest incidence: 20-34 years females
Lower incidence in those married compared with co-habiting or single.
### Young and vulnerable

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>KZN HIV Prevalence ANC (N=1029)</th>
<th>CT HIV Prevalence General Female (N=600)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤16</td>
<td>8.4%</td>
<td>12%</td>
</tr>
<tr>
<td>17-18</td>
<td>18.6%</td>
<td>17%</td>
</tr>
<tr>
<td>19-20</td>
<td>25.4%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Incidence KZN (16-35 yo) : 9% and Cape Town (16-20) yo : 8%

Karim, S, et al. CAPRISA, Bekker LG et al, DTHC.
HIV+  
HIV -ve  
24-40 years  
12-24 years.  
24-35 years.

Vicious HIV Cycle
Highly active HIV prevention.

A term coined by Prof K Holmes, University of Washington School of Medicine, Seattle, WA, USA.5
We need a biomedical Revolution!!

Why?

Source: UNAIDS 2012 HIV and AIDS estimates
What Do We Have to Address the Epidemic?

- Education and behavior modification
- Condoms, and other barrier methods
- Treatment/prevention of drug/alcohol abuse
- Clean syringes, i.e. needle exchange programs
- Interruption of mother-to-child transmission
- Circumcision for female-to-male transmission
- HIV/STI Testing
- Antiretroviral treatment as prevention
- Post-exposure prophylaxis (PEP)
- Pre-exposure prophylaxis (PrEP)*
- Topical microbicides†
- Vaccination†

*Daily Truvada®; alternate regimens still in research
†Still in research

With thanks to Carl Dieffenbach & Jeff Schouten
**HIV CARE and PREVENTION**

- Male circumcision

- Treatment of STIs
  - Grosskurth H, Lancet 2000

- Female Condoms

- Male Condoms
  - +Lube

- Microbicides for women
  - Abdool Karim Q, Science 2010

- Oral pre-exposure prophylaxis
  - Grant R, NEJM 2010 (MSM)
  - Baeten J, NEJM 2012 (Couples)
  - Paxton L, NEJM 2012 (Heterosexuals)
  - Choopanya K, Lancet 2013 (IDU)

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

- Male and female condoms

- Treatment for prevention
  - Abstinence
  - Be Faithful

- HIV Counselling and Testing
  - Coates T, Lancet 2000
  - Sweat M, Lancet 2011

- (Un)conditional cash transfers
  - Kohler HP, 2002

- Harm Reduction

- PMTCT
New technologies

• Depot PrEP (vaginal rings)
• Long Acting Injectable PrEP
• On Demand PrEP- pills, films
• Passive/Active immunisation
• Multifunctional products, eg contraception
# New biomedicals in the pipeline

<table>
<thead>
<tr>
<th>modality</th>
<th>Women</th>
<th>MSM</th>
<th>PWID</th>
<th>FSW</th>
<th>Adols</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA PrEP</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++?</td>
</tr>
<tr>
<td>Vaginal rings</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>++?</td>
</tr>
<tr>
<td>Rectal MB</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+?</td>
</tr>
<tr>
<td>Vaccines</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Passive IM</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>?</td>
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<tr>
<td>New oral agents (Maraviroc)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>?</td>
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</tbody>
</table>
Evidence for biomedicals in women
<table>
<thead>
<tr>
<th>Product</th>
<th>Study, Results published</th>
<th>Effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate ART for HIV+ partner</td>
<td>HPTN 052, 2011</td>
<td>96% (82, 99)</td>
</tr>
<tr>
<td>TDF/FTC oral PrEP</td>
<td>Partners PrEP, 2011</td>
<td>75% (55, 87)</td>
</tr>
<tr>
<td>TDF oral PrEP</td>
<td>Partners PrEP, 2011</td>
<td>67% (44, 81)</td>
</tr>
<tr>
<td>TDF/FTC oral PrEP</td>
<td>TDF2, CDC, 2011</td>
<td>62% (22, 83)</td>
</tr>
<tr>
<td>1% tenofovir gel</td>
<td>CAPRISA 004, 2010</td>
<td>39% (6, 60)</td>
</tr>
<tr>
<td>1% tenofovir gel</td>
<td>MTN003/VOICE, 2011</td>
<td>15% (-21, 40)</td>
</tr>
<tr>
<td>TDF/FTC oral PrEP</td>
<td>FEM-PrEP, 2011</td>
<td>6% (-52, 41)</td>
</tr>
<tr>
<td>TDF/FTC oral PrEP</td>
<td>MTN003/VOICE, 2011</td>
<td>-4% (-49, 27)</td>
</tr>
<tr>
<td>TDF oral PrEP</td>
<td>MTN003/VOICE, 2011</td>
<td>-49% (-129, 3)</td>
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HIV PREVENTION

Methadone

Male circumcision
- Gray R, Lancet 2007

Treatment of STIs
- Grosskurth H, Lancet 2000

Female Condoms

Male Condoms

+Lube

HIV Testing
- Coates T, Lancet 2000
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Microbicides for women
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Oral pre-exposure prophylaxis
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Post Exposure prophylaxis (PEP)
- Scheckter M, 2002

Treatment for prevention
- Cohen M, NEJM, 2011
- Donnell D, Lancet 2010
- Tanser, Science 2013

HIV PREVENTION

HIV Treatment

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HIV Vaccine Trials Network

HIV Prevention Trials Network
HIV Prevention in SSA Women: The Gap

• HIV-1 prevention interventions demonstrated to be effective in reducing HIV-1 risk are inadequate
  • **Condom use, HIV/STI testing** - Require participation/consent of male partner
  • **PrEP** - Achieving high adherence, especially among young SSA women, has been a central challenge (VOICE, Fem-PrEP)
  • **Microbicides** - Data suggest young SSA women wanted a product they could use to reduce their risk, but that microbicides did not fit into the realities of their daily lives (VOICE, FACTS 001)

• Inadequate prevention options for women unable to negotiate safe sex practices

• Developing HIV-1 prevention options that SSA women can use remains a global concern
Consider an Analogy

<table>
<thead>
<tr>
<th>PREGNANCY PREVENTION</th>
<th>HIV PREVENTION</th>
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<tbody>
<tr>
<td>Education &amp; behavior modification</td>
<td>Education &amp; behavior modification</td>
</tr>
<tr>
<td>Condoms</td>
<td>Condoms</td>
</tr>
<tr>
<td>Birth control pill</td>
<td>PrEP</td>
</tr>
<tr>
<td>“Morning-after pill”</td>
<td>PEP</td>
</tr>
<tr>
<td>Spermicide</td>
<td>Topical microbicides</td>
</tr>
<tr>
<td>Implantable birth control</td>
<td>Antibody-mediated Prevention (bnAbs)</td>
</tr>
<tr>
<td>Vasectomy/Tubal Ligation</td>
<td>Vaccination</td>
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*HIV Prevention Trials Network*
World Modern Contraceptive Prevalence by Method, Latest Year

- Female Sterilization: 223 Million
- IUDs: 169 Million
- Pill: 104 Million
- Male Sterilization: 28 Million
- Injections: 41 Million
- Condom: 90 Million

Couples Using Any Modern Method: 661 Million

Source: EPI from UNPop

Earth Policy Institute - www.earth-policy.org
Systematic review of contraceptive medicines “Does choice make a difference?”

October 2006

“It supports the contention that increased choice is associated with increased uptake and with better health outcomes (such as lower pregnancy rates and fewer STIs), and that women, given a choice, exercise it and continue use of their chosen contraceptives to a greater degree than those denied their choices.”
Seek, Test, Treat and Suppress

Oral PrEP

Vag. Rings

Passive/active vaccination

 MMC and Condoms

Universal Testing

Couples Testing

Self Testing

Community testing

PMTCT

Security

HPIN

HIV Prevention Trials Network
The HVTN 703/HPTN 081 AMP Study: Filling the Gap

AMP = Antibody Mediated Prevention

This is the idea of using an antibody made by scientists and giving it to people directly, i.e. using an intravenous (IV) infusion, to prevent HIV infections.
Combination prevention: Hep B

- Universal precautions
- Safer sex
- Vaccinate with Hep B vaccine (active)
- Passive immunization with anti Hep B immunoglobulins
Rabies

- Avoid stray dogs
- Immunize pets
- Wash wound
- Active immunization
- Passive immunization with anti rabies immunoglobulin
TAILORED, Client-Centred Prevention Packages

- CSW
- IDU
- MSM
- PMTCT

Young women
The Prevention Revolution

“Scientists have developed an array of effective tools which if implemented could reverse the AIDS epidemic”

• Professor Francoise Barré Sinoussi.
The Prevention Revolution

“Prevention activism is indispensable to overcome the epidemic”

• Archbishop Tutu.
01 December:
NATIONAL AIDS DAY
SEX BEFORE MARRIAGE IS A SIN

3 STEPS to AIDS FREE
ABSTAIN
BE FAITHFUL
CONDOMISE
#HIV
MUST
FALL
HVTN 703/HPTN 081 Protocol Team

- Chairs: Larry Corey & Mike Cohen
- co-Chairs: Sri Edupuganti & Nyaradzo Mgodi
- Protocol Team Leader & Core Medical Monitor: Shelly Karuna
- DAIDS Medical Officers: Marga Gomez & David Burns
- Statisticians: Allan DeCamp, Deborah Donnell, Peter Gilbert, Michal Juraska, Nidhi Kochar
- Laboratory Representatives: John Hural, Sue Eshleman, On Ho, David Montefiori, Vanessa Cummings, Estelle Piwowar-Manning
- VRC Representatives: Julie Ledgerwood, Barney Graham, John Mascola
- Investigator Representatives: Ken Mayer, LaRon Nelson, Manuel Villaran, Sinead Delany-Moretllwe
- Social & Behavioral Scientist: Michele Andrasik
- DAIDS Protocol Pharmacist: Scharla Estep
- Regional Medical Liaison: Simba Takuva
- Clinical Safety Specialist: Maija Anderson
- Protocol Development Manager: Carter Bentley
- FHI360/HPTN LOC Director: Niru Sista
- Senior Research Clinician: Phil Andrew
- Clinical Research Manager: Liz Greene
- Clinical Trials Manager: Carissa Karg
- SDMC Representatives: Lynda Emel, Gina Escamilla, Evangelyn Nkwopara
- Regulatory Affairs Representative: Meg Brandon
- Communications Representatives: Jim Maynard & Eric Miller
- Community Engagement Representatives: Gail Broder, Jonathan Lucas, Jontraye Davis
- Clinic Coordinators: Deb Dunbar, Lilian Saavedra, Elaine Sebastian
- CAB Representatives: Likhapha Faku, Mark Hubbard, Jim Wick
- Community Educators/Recruiters: DaShawn Usher & Luciana Kamel
- Technical Editor: Erik Schwab