Impact of biomedical prevention approaches on the implementation of HIV vaccine efficacy trials

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Outline

- HIV prevention strategies – what works?
- Technologies under development to prevent sexual transmission of HIV
- Challenges created by new biomedical prevention strategies for future HIV vaccine trials
- Conclusion
Providing AIDS treatment is important…

…so is providing AIDS prevention

Estimated number of people receiving antiretroviral therapy 2008 = 4M
Estimated number in need of antiretroviral therapy 2008 = 9.7 M

For every 2 people put on treatment, 5 more become infected

Source: UNAIDS 2009
Which interventions have been proven effective & warrant scale up for preventing sexual spread of HIV?
What works for HIV prevention: Results from RCTs with HIV incidence

- Review: 37 HIV prevention RCTs on 39 interventions:
  - PrEP: 1
  - Behavioural: 7
  - Microbicides: 12
  - Microfinance: 1
  - STI treatment: 9
  - Diaphragm: 1
  - Vaccines: 4
  - Male circumcision: 4

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumcision (Orange Farm, Rakai, Kisumu)</td>
<td>57% (42; 68) : M-A</td>
</tr>
<tr>
<td>STD treatment (Mwanza)</td>
<td>42% (21; 58)</td>
</tr>
<tr>
<td>HIV Vaccine (Thai RV144)</td>
<td>31% (1; 51)</td>
</tr>
<tr>
<td>Tenofovir gel (CAPRISA 004, South Africa)</td>
<td>39% (6; 60)</td>
</tr>
</tbody>
</table>

Source: Adapted from Padian NS, et al. Weighing the gold in the gold standard: challenges in HIV prevention research. AIDS 2010, 24:621–635
Non-vaccine technologies being studied for prevent sexual transmission of HIV

- Extending ART for prevention
- Behavioral & structural interventions
- Pre-exposure prophylaxis (PrEP)
- Microbicides
Extending ART for prevention: mathematical modeling impact

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M. Granich, Charles F. Gilks, Christopher Dye, Kevin M. De Cock, Brian G. Williams

Summary

Background Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6.7 million were still in need of treatment and a further 2.7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate ART in which the HIV

Methods We used a long-term dynamic community-level model. All HIV-infected individuals were diagnosed at the first sign of illness; ART was immediately initiated (in a model) and continued for 5 years. It has been assumed that if a patient is seen within 10 years after ART initiation, they are assumed to have been previously infected and diagnosed. We estimate the level of testing required to achieve elimination; however, the model strategy
Extending ART for prevention: clinical trial evaluation of strategy

HPTN 052
A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy Plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples

What is HPTN 052?
HPTN 052 is a Phase III, two-arm, multi-site, randomized trial to determine the effectiveness of two treatment strategies in preventing the sexual transmission of HIV in HIV-serodiscordant couples.

Based on data collected in Africa and Thailand, there is a correlation between HIV viral load (blood levels) and HIV transmission. Specifically, the higher the viral load in the blood, the more likely the chance for transmission. Antiretroviral therapy (ART) reduces the viral load in the blood, as well as in genital secretions (for both men and women), and the drugs can be detected in semen and vaginal and cervical secretions. All of this information strongly suggests that ART may make HIV-infected people less contagious. HPTN 052 compares the HIV-infection rates of two groups of HIV-serodiscordant couples. The index case of the first group starts taking ART as soon as the couple is enrolled in the study, while the index case of the second group starts taking ART when he or she has two consecutive measurements of a CD4+ cell count within or below the range of 200-250 cells/mm³, or when he or she develops an AIDS-defining illness. Both groups will receive HIV primary care and couples counseling sessions to teach them how to reduce their risk of transmission.
There is no RCT that has shown that any behavioral intervention can reduce HIV incidence – many show reductions in self-reported risk behavior.

1: Community based VCT
Knowledge of HIV status $\rightarrow$ ↓ HIV incidence
- HPTN043 – Project ACCEPT

2: Conditional cash transfers
Cash incentives $\rightarrow$ ↓ HIV incidence
- CAPRISA 007: Reducing HIV in Adolescents (RHIVA) trial

3: Positive prevention
IMB-based prevention with AIDS treatment $\rightarrow$ ↓ HIV risk
- Project Options (Study endpoint: STD incidence)
# Current antiretroviral pre-exposure prophylaxis trials underway

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Population</th>
<th>PrEP intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bangkok Tenofovir Study</strong></td>
<td>Thailand</td>
<td>2,400 IDU</td>
<td>Daily oral TDF</td>
</tr>
<tr>
<td>(CDC 4370)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>iPrEx</strong></td>
<td>Brazil, Ecuador, Peru, South Africa, Thailand, US</td>
<td>2,499 MSM</td>
<td>Daily oral TDF/FTC</td>
</tr>
<tr>
<td><strong>Partners PrEP</strong></td>
<td>Kenya, Uganda</td>
<td>4,700 discordant Couples</td>
<td>Daily oral TDF; daily oral TDF/FTC</td>
</tr>
<tr>
<td><strong>FEM-PrEP</strong></td>
<td>Kenya, Malawi, South Africa, Tanzania</td>
<td>3,900 women</td>
<td>Daily oral TDF/FTC</td>
</tr>
<tr>
<td><strong>VOICE (MTN 003)</strong></td>
<td>Malawi, South Africa, Uganda, Zimbabwe</td>
<td>5,000 women</td>
<td>Daily oral TDF; daily oral TDF/FTC; daily tenofovir gel</td>
</tr>
<tr>
<td><strong>TDF2 (CDC 4940)</strong></td>
<td>Botswana</td>
<td>1,200 heterosexual men and women</td>
<td>Daily oral TDF/FTC</td>
</tr>
<tr>
<td>Phase II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IAVI E001 &amp; E002</strong></td>
<td>Kenya, Uganda</td>
<td>150 serodiscordant couples</td>
<td>Daily oral TDF/FTC</td>
</tr>
<tr>
<td>Phase I/II</td>
<td></td>
<td></td>
<td>Daily oral TDF/FTC; Intermittent oral TDF/FTC</td>
</tr>
<tr>
<td><strong>PrEP in young MSM (ATN 082)</strong></td>
<td>United States</td>
<td>99 young MSM</td>
<td>Daily oral TDF/FTC</td>
</tr>
<tr>
<td>Phase II</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Timeline for Ongoing and Planned PrEP Trials
As of March 2009

- **FHI (West Africa)**

- **CDC 4323 (US)**

- **CDC 4370 (Thailand)**

- **CDC 4940**

- **iPrEx (multi-country)**

- **CAPRISA 004 (SA)**

- **Partners PrEP (Kenya & Uganda)**

- **FEM-PrEP (multi-country)**

- **VOICE/MTN 003 (multi-country)**

Legend:
- Oral TDF
- Oral TDF+FTC
- Topical tenofovir gel
- Oral TDF and TDF+FTC
- Oral TDF and TDF+FTC and topical tenofovir gel

- **FHI** - Phase II, daily tenofovir disoproxil fumarate (TDF) in 936 high-risk women in Cameroon, Ghana and Nigeria (funded by Gates Foundation)
- **CDC 4323** - Phase II, daily TDF among 400 MSMs in US (funded by CDC)
- **CDC 4370** - Phase II/III, daily TDF among 2,400 IDUs in Thailand (funded by CDC)
- **CDC 4940** - Phase III, daily TDF + emtricitabine (FTC) among 1,200 heterosexual men and women in Botswana (funded by CDC)
- **iPrEx** - Phase III, daily TDF+FTC among 3,000 MSM in Brazil, Ecuador, Peru, South Africa, Thailand, US (funded by NIH and Gates Foundation)
- **CAPRISA 004** - Phase IIb, pre- and post-coital 1% tenofovir gel among 980 women in South Africa (funded by USAID and LIFElab, with support from FHI and CONRAD)
- **Partners PrEP** - Phase III, daily TDF, TDF+FTC among 3,900 serodiscordant heterosexual couples in Kenya and Uganda (funded by Gates Foundation)
- **FHI FEM-PrEP** - Phase III, daily oral TDF+FTC in 3,900 high-risk women in Kenya, Malawi, South Africa (funded by USAID and Gates Foundation)
- **MTN 003/VOICE** - Phase IIb, daily tenofovir gel, oral daily TDF or oral TDF/FTC in 4,200 women in South Africa, Malawi, Uganda, Zambia, Zimbabwe (funded by NIH)
Past & Current Microbicide Clinical Trials

1st class: Surfactants
eg. N9, SAVVVY
- Kenya N-9 sponge trial
- FHI N-9 film trial
- UNAIDS COL-1492 trial
- FHI SAVVVY trial

2nd class: Polymers
eg. PRO2000, Carraguard, Cellulose Sulfate (CS)
- CONRAD CS trial
- PopCouncil Carraguard trial
- HPTN PRO2000 & BufferGel trial
- MDP 0.5% PRO2000
- 2% PRO2000

3rd class: ARVs
eg. Tenofovir gel, Dapivirine gel/ring
- CAPRISA Tenofovir gel trial
- MTN 003 VOICE trial
- IPM Dapivirine gel & ring trial

Zena Stein publishes seminal article “HIV prevention: the need for methods women can use”

'90 '92 '98 '00 '03 '04 '04 '05 '05 '07 '09 '11

Colors:
- Safe but not effective
- Increased HIV infection
- Stopped for futility
- Planned
Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim, 1,2,4† Salim S. Abdool Karim, 1,2,3,4 Janet A. Frohlich, 1 Anneke C. Grobler, 1 Cheryl Baxter, 1 Leila E. Mansoor, 1 Ayesha B. M. Kharsany, 1 Sengeziwe Sibeko, 1 Koleka P. Mlisana, 1 Zaheen Omar, 1 Tanuja N. Gengia, 1 Silvia Maarschalk, 1 Natasha Arulappan, 1 Mukelisiwe Mlotshwa, 1 Lynn Morris, 4 Douglas Taylor, 5 on behalf of the CAPRISA 004 Trial Group

The Centre for the AIDS Program of Research in South Africa (CAPRISA) 004 trial assessed the effectiveness and safety of a 1% vaginal gel formulation of tenofovir, a nucleotide reverse transcriptase inhibitor, for the prevention of HIV acquisition in women. A double-blind, randomized controlled trial was conducted comparing tenofovir gel (n = 445 women) with placebo gel (n = 444 women) in sexually active, HIV-uninfected 18- to 40-year-old women in urban and rural KwaZulu-Natal, South Africa. HIV serostatus, safety, sexual behavior, and gel and condom use were assessed at monthly follow-up visits for 30 months. HIV incidence in the tenofovir gel arm was 5.6 per 100 women-years (person time of study observation) (38 out of 680.6 women-years) compared with 9.1 per 100 women-years (60 out of 660.7 women-years) in the placebo gel arm (incidence rate ratio = 0.61; P = 0.017). In high adherers (gel adherence > 80%), HIV incidence was 54% lower (P = 0.025) in the tenofovir gel arm. In intermediate adherers (gel adherence 50 to 80%) and low adherers (gel adherence < 50%), the HIV incidence reduction was 38 and 28%, respectively. Tenofovir gel reduced HIV acquisition by an estimated 39% overall, and by 54% in women with high gel adherence. No increase in the overall adverse event rates was observed. There were no changes in viral load and no tenofovir resistance in HIV seroconverters. Tenofovir gel could potentially fill an important HIV prevention gap, especially for women unable to successfully negotiate mutual monogamy or condom use.
CAPRISA 004 Study Overview: Enrollment & Retention

Enrolled Eligible: 889

- Tenofovir: 445
  - 15 lost to follow up
  - 8 terminated early
  - Retention: 94.8%
  - Completed study: 422

- Placebo: 444
  - 10 lost to follow up
  - 12 terminated early
  - 1 died
  - Completed study: 421
HIV infection rates in the tenofovir and placebo gel groups in CAPRISA 004: 12 month Kaplan-Meier survival probability

- **Months of follow-up**:
  - 6 months: 37 HIV endpoints
  - 12 months: 65 HIV endpoints
  - Cumulative women-years: 432 vs 833
  - HIV incidence rates (Tenofovir vs Placebo): 6.0 vs 11.2%
    - 5.2 vs 10.5%
  - Effectiveness (Tenofovir vs Placebo): 47% (0.069) vs 50% (0.007)

After 12 months of gel use:
- HIV endpoints: 65
- Effectiveness: 50%
- P-value: 0.007
HIV infection rates in the tenofovir and placebo gel groups in CAPRISA 004: 24 month Kaplan-Meier survival probability

<table>
<thead>
<tr>
<th>Months of follow-up</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative HIV endpoints</td>
<td>37</td>
<td>65</td>
<td>88</td>
<td>97</td>
<td>98</td>
</tr>
<tr>
<td>Cumulative women-years</td>
<td>432</td>
<td>833</td>
<td>1143</td>
<td>1305</td>
<td>1341</td>
</tr>
<tr>
<td>HIV incidence rates (Tenofovir vs Placebo)</td>
<td>6.0 vs 11.2</td>
<td>5.2 vs 10.5</td>
<td>5.3 vs 10.2</td>
<td>5.6 vs 9.4</td>
<td>5.6 vs 9.1</td>
</tr>
<tr>
<td>Effectiveness (p-value)</td>
<td>47% (0.069)</td>
<td>50% (0.007)</td>
<td>47% (0.004)</td>
<td>40% (0.013)</td>
<td>39% (0.017)</td>
</tr>
</tbody>
</table>
### CAPRISA 004: Impact of adherence on effectiveness of tenofovir gel

<table>
<thead>
<tr>
<th></th>
<th># HIV</th>
<th>N</th>
<th>HIV incidence</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TFV</td>
<td>Placebo</td>
</tr>
<tr>
<td>High adherers</td>
<td>36</td>
<td>336</td>
<td>4.2</td>
<td>9.3</td>
</tr>
<tr>
<td>(&gt;80% gel adherence)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate adherers</td>
<td>20</td>
<td>181</td>
<td>6.3</td>
<td>10.0</td>
</tr>
<tr>
<td>(50-80% adherence)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low adherers</td>
<td>41</td>
<td>367</td>
<td>6.2</td>
<td>8.6</td>
</tr>
<tr>
<td>(&lt;50% gel adherence)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Effectiveness of tenofovir gel in HIV prevention: Sensitivity analysis

<table>
<thead>
<tr>
<th>Description</th>
<th>Effectiveness</th>
<th>CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol defined HIV endpoints (n=98)</td>
<td>39%</td>
<td>6 – 60</td>
<td>0.017</td>
</tr>
<tr>
<td>Incl HIV infection not meeting protocol def (n=98+1 = 99)</td>
<td>37%</td>
<td>4 - 59</td>
<td>0.023</td>
</tr>
<tr>
<td>PP population (n=85)</td>
<td>41%</td>
<td>7 – 63</td>
<td>0.017</td>
</tr>
<tr>
<td>Incl ineligibly enrolled (n=98+ 5=103)</td>
<td>38%</td>
<td>7 - 60</td>
<td>0.015</td>
</tr>
<tr>
<td>Incl post-trial infections (n=98 + 5 = 103)</td>
<td>41%</td>
<td>11 – 61</td>
<td>0.015</td>
</tr>
<tr>
<td>All HIV infections (n=119)</td>
<td>45%</td>
<td>19 - 63</td>
<td>0.003</td>
</tr>
</tbody>
</table>
# Impact of tenofovir gel on HSV-2 incidence

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir gel n=202*</th>
<th>Placebo gel n=224*</th>
</tr>
</thead>
<tbody>
<tr>
<td># HSV-2 infections</td>
<td>29</td>
<td>58</td>
</tr>
<tr>
<td>Women-years of follow-up</td>
<td>292.3</td>
<td>287.3</td>
</tr>
<tr>
<td>HSV-2 incidence per 100wy (95% CI)</td>
<td>9.9 (6.6, 14.2)</td>
<td>20.2 (15.3, 26.1)</td>
</tr>
</tbody>
</table>

*Note: Excludes equivocal HSV-2 results at study exit

**IRR = 0.49 (CI:0.30, 0.78);  p = 0.003**

51% protection against HSV-2 by tenofovir gel (CI: 22%-70%)
Challenges created by new biomedical prevention technologies for designs of future vaccine trials

1. Changing standard of prevention for all study participants - ? lower HIV incidence in trial

2. Equivalence or superiority of vaccines compared to other prevention strategies

3. Impact of concomitant interventions, especially antiretrovirals on HIV pathogenesis and vaccine trial endpoints such as set point viral load

4. Direct & indirect impact of prevention programs on the trial cost and complexity
1. PrEP as the Standard of Prevention

Tenofovir (gel or oral) provided to all participants (for gel – women only) in an AIDS vaccine trial

Main Challenge = ↑ sample size from ↓ incidence

Expected study size X 1/(1-effectiveness)

eg. For tenofovir gel multiply study size by:
   • 1.7 for a 30 month endpoint or
   • 2 for a 12 month endpoint

Sample size calculations courtesy of Dr Doug Taylor, FHI
HIV prevalence in pregnant women in rural Vulindlela (2005-2008) despite intensive HIV prevention

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>HIV Prevalence (%) (N=1237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤16</td>
<td>10.6</td>
</tr>
<tr>
<td>17-18</td>
<td>21.3</td>
</tr>
<tr>
<td>19-20</td>
<td>33.0</td>
</tr>
<tr>
<td>21-22</td>
<td>44.3</td>
</tr>
<tr>
<td>23-24</td>
<td>51.1</td>
</tr>
</tbody>
</table>
2. PrEP as an active-control

Randomize to vaccine candidate or Tenofovir (oral or gel) to assess relative effectiveness

Challenges:

- Incidence rate in control arm reduced; larger study sample size required
- May not be possible to blind
- May not be ethical
Impact of tenofovir gel on HIV incidence in CAPRISA 004: implications for future trials

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir Gel N=445</th>
<th>Placebo Gel N=444</th>
</tr>
</thead>
<tbody>
<tr>
<td># HIV infections</td>
<td>38</td>
<td>60</td>
</tr>
<tr>
<td>Women-years (# women)</td>
<td>680.6 (445)</td>
<td>660.7 (444)</td>
</tr>
<tr>
<td>HIV incidence (per 100 women-years)</td>
<td>5.6</td>
<td>9.1</td>
</tr>
</tbody>
</table>
Superiority trials with active control

Assume background incidence of 5 per 100 per- yrs, and tenofovir gel 40% effective (90% power)

<table>
<thead>
<tr>
<th>Effectiveness (Vaccine vs Tenofovir gel)</th>
<th>HIV endpoints required</th>
<th>Study Size (person-years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25%</td>
<td>510</td>
<td>19,500</td>
</tr>
<tr>
<td>33%</td>
<td>260</td>
<td>10,400</td>
</tr>
<tr>
<td>50%</td>
<td>90</td>
<td>4,000</td>
</tr>
</tbody>
</table>

Sample size calculations courtesy of Dr Doug Taylor, FHI
Non-Inferiority Trials (90% Power)

* Assuming background incidence rate of 5 per 100 per-yrs

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Events required to rule out RR &gt;1.25</th>
<th>Study size (person-years)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFV Vaccine</td>
<td>40%</td>
<td>28,500</td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>9,500</td>
</tr>
<tr>
<td></td>
<td>60%</td>
<td>4,400</td>
</tr>
</tbody>
</table>

Seek to show that the vaccine is equally effective or at most a small and acceptable amount inferior to Tenofovir (e.g. HR=1.25)

Sample size calculations courtesy of Dr Doug Taylor, FHI
3. Potential impact on vaccine endpoints

Tenofovir (gel or oral) could impact on some AIDS vaccine endpoints

Challenges – what if tenofovir:
- reduces viral load set point
- impacts genetic bottleneck
- impacts on immune markers
- alters natural disease progression
Impact of tenofovir gel on initial viral load in seroconvertors in CAPRISA 004

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of events</td>
<td>38</td>
<td>60</td>
</tr>
<tr>
<td>Log mean viral load</td>
<td>4.65</td>
<td>4.30</td>
</tr>
<tr>
<td>Range (IQR)</td>
<td>4.04 - 5.39</td>
<td>3.56 – 5.17</td>
</tr>
<tr>
<td>p-value</td>
<td>p=0.15</td>
<td></td>
</tr>
</tbody>
</table>
Tenofovir gel exposure did not affect the HIV genetic bottleneck in CAPRISA 004

<table>
<thead>
<tr>
<th></th>
<th>TNF</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>17 (77%)</td>
<td>6</td>
</tr>
<tr>
<td>Multi</td>
<td>5 (23%)</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from Carolyn Williamson, UCT
Impact of tenofovir gel on CD4 IFNγ responses in CAPRISA 004

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir</th>
<th>Placebo</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>17</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>*Age</td>
<td>24</td>
<td>23</td>
<td>0.69</td>
</tr>
<tr>
<td>*Days post infection</td>
<td>85</td>
<td>64</td>
<td>0.30</td>
</tr>
<tr>
<td>*CD4 count post infection</td>
<td>464</td>
<td>510</td>
<td>0.17</td>
</tr>
<tr>
<td>*Initial CD4 count</td>
<td>454</td>
<td>556</td>
<td>0.11</td>
</tr>
<tr>
<td>*Log Viral Load post infection</td>
<td>4.96</td>
<td>4.51</td>
<td>0.72</td>
</tr>
<tr>
<td>*Initial Viral Load</td>
<td>4.66</td>
<td>4.42</td>
<td>0.58</td>
</tr>
</tbody>
</table>

* = Median

Women who acquired HIV infection in the tenofovir arm had greater CD4 cell responses by gamma interferon elispot assay

Similar responses are sought in HIV vaccine trials

HIV specific CD4 IFNγ responses

Data from M. Mureithi and M. Altfeld
4. Impact of prevention programs on the trial cost and complexity

Tenofovir gel is not available – will need to make it for a trial

Tenofovir pills are available and are relatively low cost

Challenges – expansion of prevention standard would entail:

- Additional visits, HIV testing, counselling, etc
- Additional safety assessments
- Higher costs
The prevention gap: Inclusion of comprehensive prevention will need trial-specific implementation

Access to existing HIV prevention methods, 2007

- 8% injecting drug users have access to prevention services
- 9% risky sex acts worldwide are undertaken while using a condom
- 9% men who have sex with men have access to prevention services
- 11% of adults in developing countries know their HIV status
- 11% HIV-infected pregnant women in developing countries receive ARV for pMTCT
- <20% commercial sex workers can access prevention services
- <20% of people with STI have access treatment
- 60% of injections administered in health care settings are safe

Conclusion

- AIDS vaccine remains a high priority amidst other biomedical prevention technologies under study
- CAPRISA 004 - proof of concept for topical PrEP. More results of PrEP trials of tenofovir (gel or oral) will become available over the next 2 years.

Impact of new biomedical prevention interventions on the design of future HIV vaccine trials:
- Higher prevention standard in vaccine trials
- Increased sample size
- May complicate vaccine endpoint measurement
- Increased complexity in trial implementation
- Higher costs
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- A special tribute to the many thousands of people who participate in HIV microbicide & vaccine trials