ARVs for prevention in at-risk populations: Microbicides

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Salim S Abdool Karim
Director: CAPRISA
Pro Vice-Chancellor (Research): University of KwaZulu-Natal
Professor in Clinical Epidemiology, Columbia University
Adjunct Professor of Medicine, Cornell University
Associate: Ragon Institute of MGH, MIT and Harvard
HIV prevalence in school boys & girls in rural South Africa (Grades 9 & 10)

<table>
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<tr>
<th>Age Group</th>
<th>HIV Prevalence (Oct/Nov 2010) % (95% Confidence Interval)</th>
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## HIV prevalence in young pregnant women in rural Vulindlela, South Africa (2009-2012)

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<th>Age Group (Years)</th>
<th>HIV Prevalence (N=1029)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤16</td>
<td>8.4</td>
</tr>
<tr>
<td>17-18</td>
<td>18.6</td>
</tr>
<tr>
<td>19-20</td>
<td>25.4</td>
</tr>
<tr>
<td>21-22</td>
<td>32.8</td>
</tr>
<tr>
<td>23-24</td>
<td>44.8</td>
</tr>
</tbody>
</table>
High rates of HIV among the key populations of young women in Africa


Young women have up to 8 times more HIV than men

Source: Adapted from UNAIDS 2012
HIV risk in young women in Africa

• Pressure to have sex at a young age
  ▪ for money or favours
  ▪ peer pressure
  ▪ flattering to be desired by an older man

• Poor internalisation of HIV risk
  ▪ Knowledge of HIV status low & “AIDS affects other people”
  ▪ Lack of sense of a future (Live for today)
  ▪ Change partners regularly or have multiple partners

• Which of the HIV prevention tools are going to be effective in young African women?
  ▪ Abstinence
  ▪ Behaviour (Be faithful)
  ▪ Condoms (male & female)
  ▪ Circumcision (Medical Male)
  ▪ TasP
  ▪ ARV prophylaxis (PrEP / Microbicides)
Overview: microbicide effectiveness trials

1\textsuperscript{st} class: Surfactants  
eg. N9, SAVVY
- Kenya N-9 sponge trial
- FHI N-9 film trial
- UNAIDS COL-1492 trial
- FHI SAVVY trial

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

3\textsuperscript{rd} class: ARVs  
eg. TFV gel & DPV ring
- CAPRISA 004 Coital Tenofovir gel trial
- MTN003 –VOICE Daily Tenofovir gel  
  Daily Tenofovir tablets & Daily Truvada trial
- FACTS 001 Coital Tenofovir gel trial
- CAPRISA 008 Tenofovir gel implementation trial
- MTN & IPM Dapivarine ring trials

Zena Stein publishes seminal article “HIV prevention: the need for methods women can use”
Key Lesson: Adherence is essential

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th># HIV</th>
<th>N</th>
<th>HIV incidence</th>
<th>Effect</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High adherers</strong> (&gt;80% gel adherence)</td>
<td>36</td>
<td>336</td>
<td>4.2</td>
<td>9.3</td>
<td>54%</td>
</tr>
<tr>
<td><strong>Intermediate adherers</strong> (50-80% adherence)</td>
<td>20</td>
<td>181</td>
<td>6.3</td>
<td>10.0</td>
<td>38%</td>
</tr>
<tr>
<td><strong>Low adherers</strong> (&lt;50% gel adherence)</td>
<td>41</td>
<td>367</td>
<td>6.2</td>
<td>8.6</td>
<td>28%</td>
</tr>
</tbody>
</table>

CAPRISA 004 was developed… …”after extensive consultation with international scientific experts and review of monkey challenge data.” “Just as importantly, it followed detailed consultation with the communities involved.”

*Source: Abdool Karim S, Abdool Karim Q, Nature, 446; 2007*

Relationship between effectiveness and adherence in microbicide & PrEP trials

Pearson correlation = 0.86, p=0.003

- CAPRISA 004
- iPrEX
- TDF2
- PartnersPrep (TDF)
- PartnersPreP (FTC)
- FemPrEP
- VOICE (TDF)
- VOICE (Truvada)
- VOICE (TFV gel)
# Tenofovir gel effectiveness by various measures of adherence

<table>
<thead>
<tr>
<th>Estimated effectiveness</th>
<th>Estimated adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MTN 003 (VOICE)</strong></td>
<td></td>
</tr>
<tr>
<td>14.5%</td>
<td>23%</td>
</tr>
<tr>
<td>(based on detectable tenofovir in plasma samples)</td>
<td></td>
</tr>
<tr>
<td><strong>CAPRISA 004</strong></td>
<td></td>
</tr>
<tr>
<td>39%</td>
<td>Estimated 50% use at last sex act</td>
</tr>
<tr>
<td>54%</td>
<td>&gt;80% of sex acts covered by 2 applicators</td>
</tr>
<tr>
<td></td>
<td>(based on applicator counts &amp; self-reported sex)</td>
</tr>
<tr>
<td>74%</td>
<td>Detection of high concentrations of tenofovir (&gt;1000ng/ml) in CVL</td>
</tr>
<tr>
<td>90%</td>
<td>Case-control analysis based on tenofovir concentrations in CVL</td>
</tr>
</tbody>
</table>
WHO has started working on guidelines for tenofovir gel implementation

- 2004: CAPRISA 004 Clinical Phase
- 2005-2006: CAPRISA results & CSR
- 2007: VOICE Clinical Trial
- 2008-2009: FACTS 001
- 2010-2011: FACTS CSR
- 2012: WHO guideline development
- 2013: Global TFV gel implementation strategy development
- 2014: Regulatory approval
- 2015-2016: Launch

WHO has started working on guidelines for tenofovir gel implementation
Microbicide product pipeline

- ARVs in gels, rings, films & SILCS diaphragm:
  - Multi-purpose prevention technologies
    A single product, configured for at least two SRH prevention indications:
    - Contraception
    - Protection against HIV
    - Protection against other STIs eg. BV, HSV-2
HIV prevalence among MSM in Africa

HIV prevalence in MSM:
Range:
6.2% in Egypt to 30.9% in Cape Town

MTN is conducting a phase II trial of a rectal formulation of tenofovir gel

Conclusion

• Concept of microbicides now proven - 20 years after first proposed & 18 years after first human trials

• Results of FACTS 001 (confirmatory trial) eagerly awaited - next step towards licensure of tenofovir gel

• Antiretroviral based microbicides address a gender dynamic in HIV as a women-initiated technology

• New formulations & multipurpose technology approaches hold new hope for improving adherence

• Several new products are in the pipeline while the effort to get tenofovir gel to women is in progress
The 6 falsehoods of effective ARV prophylaxis for HIV prevention

1. ARV MB/PrEP should only be used for prevention after all eligible AIDS patients are on treatment
2. It is not safe to give ARV MB/PrEP to healthy people
3. Data on the effectiveness of MB/PrEP, especially in women, are inconsistent & so efficacy is in doubt
4. Healthy people will not adhere to MB/PrEP
5. ARVs in MB/PrEP will undermine future AIDS treatment by causing drug resistance
6. MB/PrEP users will increase their HIV risk by stopping their use of condoms