Clinicopathological Conference at the Annual Workshop in Advanced Clinical Care, Durban
October 1, 2010

Prof WD Francois Venter, FCP (SA)
University of the Witwatersrand, Johannesburg,
Thumbi Ndung’u, BVM, PhD
Doris Duke Medical Research Institute,
Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban

Quarraisha Abdool Karim PhD
Centre for the AIDS Programme of Research in South Africa (CAPRISA)
“A 19-year-old South African woman with headache, fatigue and vaginal discharge.”

Fundisiwe Chonco, BSc, MBChB (UCT)
University of KwaZulu-Natal, Durban, South Africa
Case Presentation

• A 19-year-old woman developed vaginal discharge, headache, fatigue, sore throat and anorexia.
• 5 days later, she was seen at a local clinic.
• **BACKGROUND:** Born in South Africa and lived in a bricked house with running water and electricity, and attended school.
• **PMH:** History of an accident in childhood, with developmental delay and chronic neurological deficits. No history of sexual transmitted diseases.
1st clinic visit

PE: vital signs normal, vaginal discharge present. Rest of exam normal except for her chronic stable neurological deficits.

Treatment:
• Doxycycline 100 mg twice daily for 7 days
• Metronidazole 2 gm orally once
• Ceftriaxone 250 mg intramuscularly once
1st clinic visit, continued

Studies:

• Rapid HIV-1/2 tests (Bioline and Sensa) performed on whole blood (finger-prick). Results: negative.

• A blood sample of 5mls in an EDTA tube obtained for further testing

• Referred to another clinic (McCord Hospital, Durban, affiliated with Massachusetts General Hospital) for follow up.
12 days later

• Headache, fatigue, sore throat and vaginal discharge persisted.

Additional history:

• Sexually active four times in past, with 25-year-old boyfriend of 6 months. Boyfriend had refused to use condoms because of decreased sensation.
2\textsuperscript{nd} clinic visit, continued

PE: Weight 73kg, temperature 36.0\textdegree C, blood pressure 93/59 mm Hg, pulse 82 beats/min. Genital exam: small amount of malodorous vagina discharge, no other lesions. The remainder of the exam was consistent with her long-term neurological deficits.

Studies: Two additional rapid HIV screening tests (Determine and Abbott) performed on the blood drawn at the visit to the 1\textsuperscript{st} clinic. Results: negative.
2nd clinic visit, continued

- Counseled on safe sex practices and encouraged to bring her boyfriend for STD treatment and HIV testing. No treatment was given.
- Additional blood drawn for further testing and follow up scheduled.
14 days later

During the next 14 days:

– headache, fatigue, anorexia, sore throat and vaginal discharge resolved
– a painful genital ulcer developed

She returned to the clinic.
• She reported no sexual contact since her last visit, and had no previous history of oral or genital ulcers.
PE: Afebrile, with normal vital signs. Tender lymph nodes (1cm in diameter) in her submental, posterior cervical, epitrochlear regions. There was a single painful ulcer (5 mm by 10 mm) on the left labia majora, without induration.

Studies:
• Rapid plasma reagin (RPR) was negative.

Treatment:
• Penicillin G benzathine 2.4 million units intramuscularly once
• Erythromycin 500 mg four times per day for 7 days
• Diagnostic test results were reviewed.
Differential Diagnosis

Prof WD Francois Venter, FCP (SA)

Senior Director, HIV Management Cluster, Reproductive Health and HIV Research Unit (RHRU)
Associate Professor, Department of Medicine
University of the Witwatersrand, Johannesburg, South Africa
Diagnostic Test Results
Thumbi Ndung’u, BVM, PhD

Associate Professor in HIV/AIDS Research;
Director, HIV Pathogenesis Programme (HPP)
Doris Duke Medical Research Institute,
Nelson R. Mandela School of Medicine,
University of KwaZulu-Natal, Durban, South Africa
Detection of HIV Infection

- Detect the virus itself or the body’s specific reaction to the virus

- Tests for the virus itself: DNA PCR, RNA PCR, p24 antigen, virus culture- these tests are expensive and difficult to do. Therefore reserved for blood screening, infant diagnosis and research

- Body’s reaction: usually detect HIV specific antibody- Rapid tests, ELISA, Western blot, urine tests, saliva tests.
Window Period

- Period between infection and first reliable detection of HIV by lab test

- Window period varies by test and by individual

- The majority of infected individuals are positive by ELISA, antigen and/or DNA/RNA tests by 6-8 weeks after infection
Natural History and Laboratory Staging of HIV Infection

Eclipse Phase

- I
- II
- III
- IV
- V
- VI

Western blot +/+ (p31+)
Western blot +/-(p31-)
ELISA+
p24Ag+
v RNA+

Viral RNA cutoff 50 copies/ml
Ultrasensitive Viral RNA cutoff 1-5 copies/ml

Days following HIV-1 transmission

(Fiebig, AIDS 2003)
Minimum Time from Infection to First Detection of HIV-1 Markers

KEY:
- **NO DETECTION**
- **DETECTION OF HIV**

Detection of HIV: Days after infection

- **ELISA**
- **p24**
- **DNA PCR**
- **RNA**
Diagnosis in Adults

• In adults, diagnosis of HIV infection is best determined by the detection of antibodies (markers) to the virus in blood.

• The antibodies are specific for particular virus proteins and are unique to HIV.
Easiest Methods for Sero-diagnosis of HIV Infection

- Rapid tests
- Non-invasive testing methods (saliva or urine)
Rapid Tests

- Quick, cheap, easy to use
- Easy to store
- Lab not required
- Combinations of rapid tests highly sensitive and specific
- However, interpretation requires trained personnel
Rapid Tests

• Quick, cheap, easy to use
• Easy to store
• Lab not required
• Combinations of rapid tests highly sensitive and specific
• However, interpretation requires trained personnel
Rapid Test Algorithm for HIV Diagnosis

2 Parallel Rapid Tests Negative

Patient uninjected or in window period of infection
HIV Rapid Test Algorithm (contd.)

- 2 Parallel Rapid Tests Positive → Patient infected
- Discordant Parallel Rapid Tests (positive/negative)
- Repeat Rapid tests or tie-breaker →
  - Positive → Patient infected
  - Negative → Patient uninfected or in window period of infection
- Discordant → ELISA or Western blot
  - Positive → Indeterminate
  - Negative → Re-draw blood and repeat tests
ELISA Method

- (ELISA) Enzyme Linked Immunosorbent Assay

- Detects antibodies directed at a specific HIV protein or fragment- e.g. Gag or Envelope

- Most commonly used laboratory method- high sensitivity and specificity
Western Blot

- Most commonly used confirmatory test
- Detects antibodies directed at specific HIV proteins- envelope and core proteins
Diagnosis in Infants

- Diagnosis of HIV by antibody testing in infants under 18 months is complicated by the presence of maternal antibodies.

- Hence detection of HIV nucleic acid in infant blood is done by DNA PCR.

- PCR based on cellular proviral HIV DNA provides a qualitative result: Positive or Negative.
Plasma pooling for HIV RNA detection

HIV-1 RNA detected, proceed to 4 pools of 6 each

No RNA detected - report all HIV negative
If pool of 24 is positive…

Make 4 pools of 6 samples each

If pool is +ve…

Quantify viral load in individual samples (this will be quantitative)
Interpretation of pooling results

• This depends on study algorithm or purpose of pooling:
   In research protocols to identify acute infection every suspect is eligible for inclusion
   In vaccine studies, you are looking to confirm breakthrough infection so the bar may be set higher e.g. ≥1000 copies/ml
   In blood bank, any suspect has to be considered positive.
Diagnostic laboratory results

- Rapid tests results at clinic:
  - Sensa- negative, Bioline- negative

- Rapid results at laboratory:
  - Abbott Determine- negative, Unigold-negative

- ELISA (SD HIV1/2, Standard Diagnostics)-3rd generation- negative

- Western blot (Genetic Systems, Biorad)- negative
Diagnostic laboratory results

- Plasma pooling of 6 samples was positive by Roche Ampliscreen assay

- Deconstruction and viral load measurement of individual samples in pool - yielded one +ve sample with viral load of 12,445 copies/ml

- All other samples in pool had no HIV-1 RNA signal detected
## Sequential Western blot analysis

<table>
<thead>
<tr>
<th>Estimated No. of days post infection*</th>
<th>14</th>
<th>26</th>
<th>40</th>
<th>55</th>
</tr>
</thead>
<tbody>
<tr>
<td>gp160</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>gp120</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>p65</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>p55/51</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>gp41</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>p40</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>p31</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>p24</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>p18</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>-/+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interpretation#</th>
<th>Negative</th>
<th>Indeterminate</th>
<th>Positive</th>
<th>Positive</th>
</tr>
</thead>
</table>

Final Diagnosis

Acute HIV infection in a young woman in KwaZulu-Natal, South Africa
Discussion of Management

Prof WD Francois Venter, FCP (SA)
Discussion of Epidemiology

Quarraisha Abdool Karim, PhD
Centre for the AIDS Programme of Research in South Africa (CAPRISA),
Associate Professor in Public Health and Family Medicine,
Nelson R. Mandela School of Medicine, University of KwaZulu-Natal,
South Africa

Associate Professor of Clinical Epidemiology,
Mailman School of Public Health, Columbia University, New York, USA

Vivek Naranbhai, BSc.MedSci(Hons), MBChB
Centre for the AIDS Programme of Research in South Africa (CAPRISA)
Overview

• Epidemiology of HIV in South Africa

• Existing and new management options
The South African HIV Epidemic – A generalised, hyperendemic epidemic!

Source: Data from South African Department of Health Antenatal Surveys. www.doh.gov.za/
Age & Gender profile of HIV infection in South Africa – a key driver of the HIV epidemic

Importance of young women in the HIV epidemic in South Africa

National Youth survey
Pettifor et al. AIDS 2005 Vol 19, No 14
HIV prevalence in pregnant women in rural Vulindlela, South Africa (2005-2008)

<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>
Partner Age of Pregnant ANC clients <25 years and HIV prevalence: 2004-2008

HIV Prevalence in women (%)  
Partner’s Age in years

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;20</th>
<th>20-24</th>
<th>25-29</th>
<th>&gt; 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-16</td>
<td>6.7</td>
<td>12.7</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>17-18</td>
<td>14.6</td>
<td>22.6</td>
<td>41.7</td>
<td></td>
</tr>
<tr>
<td>19-20</td>
<td></td>
<td>29.2</td>
<td>46.3</td>
<td>44.4</td>
</tr>
<tr>
<td>21-22</td>
<td></td>
<td>37.9</td>
<td>53.6</td>
<td>64.0</td>
</tr>
<tr>
<td>23-24</td>
<td></td>
<td>55.5</td>
<td>51.9</td>
<td>74.3</td>
</tr>
</tbody>
</table>
### HIV Pre-Prevention Trial Cohorts in KwaZulu-Natal: 2005 - 2006

<table>
<thead>
<tr>
<th></th>
<th>Rural (FP -05)</th>
<th>Urban (STI)</th>
<th>Urban (CSW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Screened</td>
<td>782</td>
<td>1259</td>
<td>776</td>
</tr>
<tr>
<td>HIV prevalence (%)</td>
<td>30.2</td>
<td>59.3</td>
<td>59.4</td>
</tr>
<tr>
<td>Enrolment rate/month</td>
<td>27</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td>p-y follow up</td>
<td>300</td>
<td>52</td>
<td>201</td>
</tr>
<tr>
<td>Incidence rate (1/100pyrs)</td>
<td>7.4</td>
<td>5.8</td>
<td>7.5</td>
</tr>
</tbody>
</table>

CAPRISA, unpublished
Summary 1

• South Africa: a generalised, hyperendemic HIV epidemic
• Disproportionate burden of HIV infection in young woman
• Age-sex distribution of HIV – key driver of transmission
• Case provides a face to the epidemic:
  – 19 year old female
  – 25 year old male partner
  – Few sexual encounters (four)
  – STI: vaginal discharge + ulcer
HIV Transmission Dynamics - What do we know?
HIV Acquisition risk per sex act

**Male-to-female**

- Kim (1988)\textsuperscript{77} 14
- Jackson (1989)\textsuperscript{79} 17
- Lawrence (1989)\textsuperscript{80} 19
- Kim (1990)\textsuperscript{81} 55
- Allen (1992)\textsuperscript{62} 30
- Downs (1996)\textsuperscript{87} 73
- Downs (1996)\textsuperscript{87} 377
- Hira (1997)\textsuperscript{70} 80
- Padian (1997)\textsuperscript{15} 360
- Saracco (1997)\textsuperscript{18} 627
- Shiboski (1998)\textsuperscript{16} 31
- Duerr (2000)\textsuperscript{67} 78
- Ryder (2000)\textsuperscript{71} 92
- Fidel (2001)\textsuperscript{72} 535
- Gray (2001)\textsuperscript{19} 97
- Roth (2001)\textsuperscript{63} 43
- Gilbert (2003)\textsuperscript{73} 1029
- Marinovitch (2003)\textsuperscript{89} 66
- Kimani (2008)\textsuperscript{75} 687

**Pooled**

Test for heterogeneity: $Q=559.0$ ($p<0.0001$)

- 0.047% (0.000–0.138)
- 0.075% (0.000–0.221)
- 0.075% (0.000–0.222)
- 0.134% (0.051–0.217)
- 0.318% (0.064–0.573)
- 0.150% (0.046–0.254)
- 0.050% (0.030–0.070)
- 0.225% (0.045–0.406)
- 0.090% (0.050–0.100)
- 0.072% (0.049–0.095)
- 0.090% (0.040–0.200)
- 0.240% (0.150–0.320)
- 0.517% (0.103–0.931)
- 0.988% (0.773–1.203)
- 0.090% (0.047–0.133)
- 0.240% (0.000–0.572)
- 0.031% (0.022–0.040)
- 0.018% (0.000–0.054)
- 0.082% (0.072–0.091)
- 0.124% (0.078–0.199)
HIV transmission risk in relation to viral load

HIV transmission risk in relation to viral load

![Graph showing HIV transmission risk in relation to viral load.](image)

HIV transmission risk in relation to disease stage

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>RR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1 (reference)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Early</td>
<td>9.17 (4.47–18.81)</td>
<td>-</td>
</tr>
<tr>
<td>Late</td>
<td>7.27 (4.45–11.88)</td>
<td>-</td>
</tr>
<tr>
<td>Setting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-income countries</td>
<td>1 (reference)</td>
<td>-</td>
</tr>
<tr>
<td>High-income countries</td>
<td>0.79 (0.49–1.29)</td>
<td>-</td>
</tr>
</tbody>
</table>

Boily et al. Lancet Infectious Diseases 2009
HIV transmission risk in relation to GUD

Boily et al. Lancet Infectious Diseases 2009
Summary 2

• Enhancing HIV transmission
  – Partner age
  – Partner HIV infected or with AIDS
  – Elevated viral load
  – Concurrent ulcerative STI

• Could we have prevented infection of
  – HIV?
  – HSV-2?

• Can we prevent onward transmission? (positive prevention)
What works for HIV prevention? Results from RCTs with HIV incidence

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

Study

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

Preventing sexual spread of HIV:

- Existing accepted proven HIV prevention strategies - ABCCC:
  - Abstinence
  - Behaviour (Be faithful)
  - Condoms (Male & Female)
  - Counselling and Testing
  - Circumcision (Medical Male)

Which of these are prevention tools for young women in Africa?
Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,1,2*† Salim S. Abdool Karim,1,2,3* 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 Gengiah,1 Silvia Maarschalk,1 Natasha Arulappan,1 Mukelisiwe Mlotshwa,1 Lynn Morris,4 Douglas Taylor,5 on behalf of the CAPRISA 004 Trial Group‡

1Centre for the AIDS Program of Research in South Africa (CAPRISA), Durban, South Africa. 2Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA. 3University of KwaZulu-Natal, Durban, South Africa. 4National Institute for Communicable Diseases, Johannesburg, South Africa. 5FHI, North Carolina, USA.

*These authors contributed equally to this work.

†To whom correspondence should be addressed. E-mail: caprisa@ukzn.ac.za

‡The members of the CAPRISA 004 Trial Group appear at the end of this paper.

The CAPRISA 004 trial assessed 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 region which accounts for 70% of global burden of Human Immunodeficiency Virus (HIV) infection (1). Current HIV prevention behavioral messages on abstinence, faithfulness and condom promotion have had limited impact on HIV

Available for download from: [http://www.sciencemag.org/sciencexpress/recent.dtl](http://www.sciencemag.org/sciencexpress/recent.dtl)
CAPRISA 004 assessed the safety and effectiveness of 1% tenofovir gel

- BAT 24 coitally-related gel use
  - Insert 1 gel up to 12 hours **Before sex,**
  - Insert 1 gel as soon as possible within 12 hours **After sex,**
  - No more than **two doses in 24 hours**

HIVNET 012 nevirapine regimen

- **Onset of labour:** 12 hrs
- **Delivery:** 72 hrs
- **asap**

CAPRISA 004 tenofovir gel regimen

- 12 hrs
- **asap** 12 hrs
HIV infection rates in the Tenofovir and placebo gel groups: Kaplan-Meier survival probability

- **Probability of HIV infection**
  - **0.0**
  - **0.5**
  - **1.0**
  - **1.5**
  - **2.0**
  - **2.5**
- **Years**
  - 6
  - 12
  - 18
  - 24
  - 30
- **Cumulative HIV endpoints**
  - 37
  - 65
  - 88
  - 97
  - 98
- **Cumulative women-years**
  - 432
  - 833
  - 1143
  - 1305
  - 1341
- **HIV incidence rates (Tenofovir vs Placebo)**
  - 6.0 vs 11.2
  - 5.2 vs 10.5
  - 5.3 vs 10.2
  - 5.6 vs 9.4
  - 5.6 vs 9.1
- **Effectiveness (p-value)**
  - 47% (0.069)
  - 50% (0.007)
  - 47% (0.004)
  - 40% (0.013)
  - 39% (0.017)

**Graph:**
- **Tenofovir**
- **Placebo**
- **p=0.017**
Effectiveness of tenofovir gel in preventing HIV infection

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir gel</th>
<th>Placebo gel</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</td>
<td>5.6</td>
<td>9.1</td>
</tr>
<tr>
<td>(per 100 women-years)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Incidence rate ratio: 0.61 (CI: 0.4 to 0.94); p = 0.017

39% lower HIV incidence in tenofovir gel group
# Impact of adherence on effectiveness of tenofovir gel

<table>
<thead>
<tr>
<th>Adherence Level</th>
<th>N</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High adherers</strong> (&gt;80% gel adherence)</td>
<td>336</td>
<td>54%</td>
</tr>
<tr>
<td><strong>Intermediate adherers</strong> (50-80% adherence)</td>
<td>181</td>
<td>38%</td>
</tr>
<tr>
<td><strong>Low adherers</strong> (&lt;50% gel adherence)</td>
<td>367</td>
<td>28%</td>
</tr>
</tbody>
</table>
What works for HIV prevention: Results from RCTs with HIV incidence

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<td></td>
</tr>
<tr>
<td>Microbicide</td>
<td>39% (6; 60)</td>
</tr>
<tr>
<td>(CAPRISA 004 tenofovir gel)</td>
<td></td>
</tr>
</tbody>
</table>
Global epidemic of HSV-2 infection

- High prevalence of HSV-2 infection
  - ~ 20% in sexually active adults globally
  - ~ 50 - 60% in South African sexually active adults
  - ~ 80% in HIV infected men and women globally

- Commonest cause of genital ulcer disease

- HSV-2 infection almost entirely asymptomatic
  - up to 90% of HSV-2 positive have no prior GUD

- Acyclovir & other antivirals effective HSV-2 treatment (viral suppression) but do not prevent or cure HSV-2
## Impact of tenofovir gel on HSV-2 incidence

<table>
<thead>
<tr>
<th></th>
<th>Tenofovir gel</th>
<th>Placebo gel</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</td>
<td>9.9</td>
<td>20.2</td>
</tr>
</tbody>
</table>

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

\[
\text{IRR} = 0.49 \quad (\text{CI}: 0.30, 0.78); \quad p = 0.003
\]

51% protection against HSV-2 by tenofovir gel (CI: 22%-70%)
Summary of CAPRISA 004

• Safety
  – No substantive safety concerns
  – No tenofovir resistance identified
  – Safe in Hepatitis B virus infected women
  – No evidence of risk compensation / behavioral disinhibition

• Proof of concept that tenofovir gel can prevent HSV-2 infection in women
  – 51% reduction in HSV-2

• Proof of concept that tenofovir gel can prevent HIV infection in women
  – 50% reduction in HIV after 1 year of tenofovir gel use
  – 39% protection after 30 months of gel use
  – 54% effective if adherence > 80%
Next steps post CAPRISA 004: Getting tenofovir gel into women’s hands

• Mathematical modeling of the CAPRISA 004 results indicate that over the next 2 decades in South Africa alone:
  – about 1,323,000 new HIV infections can be prevented
  – about 826,000 deaths could be averted
  – the potential long-term synergistic effect of tenofovir gel on HSV-2 could substantially enhance the impact on HIV

• Four parallel steps
  – Confirmation of CAPRISA 004 results
    • VOICE
    • FACTS
  – Licensure of Tenofovir Gel
  – Implementation Science research for scale-up
  – Basic Science to better understand results
    • Inform how to enhance findings
Do we have proven positive prevention programs?

11 of 12 rigorous RCTs of Interventions that target people living with HIV/AIDS demonstrate risk reduction

Conclusions

• Case study typifies the South African HIV epidemic
  – Young women <25 years bear a disproportionate burden of HIV infection
  – Age of partner is associated with higher HIV risk in young women
  – In presence of an STI, increased transmission probability
  – High HIV viral load & increased probability of transmission

• Need for HIV prevention methods for women
  – CAPRISA 004 provides evidence for first women initiated method
  – Also promise of an HSV-2 preventive tool
  – Much more needs to be done to get a microbicide into women’s hands

• Need for combination prevention options that target men and women to alter current epidemic trajectories
  – Knowledge of HIV status
  – Male circumcision
  – Microbicide
  – Test and treat/treatment as prevention
  – Positive prevention
  – Enhanced sexual reproductive health services
Followup

Fundisiwe Chonco, BSc, MBChB
Follow up

• She is healthy

• No new/ recurrent sexual transmitted diseases

• She hasn’t started HAART

• She accepted and disclosed her HIV status to her mum and her cousin