HIV transmission and sex: Why can’t we get it right?

“aka: “How much of this is behaviour and how much is inherent risk?”

Francois Venter
Deputy Executive Director, WRHI
Wits Reproductive Health and HIV Institute
Associate Professor, Department of Medicine
University of the Witwatersrand, Johannesburg, South Africa

Thanks to David Wilson, Clinical Care Options, Helen Rees, Marlise Richter, Dan Savage, Daniel Halperin, Soul City, Mike Cohen, Laurie Bruns, Matthew Chersich, Samantha Barichievy, Mark Lurie
CONCENTRATED AND GENERALIZED EPIDEMICS GLOBALLY

2% population; 33% HIV infections
Warning

• Not for delicate sensibilities
• Too many slides, talk will jump all over the place

“It’s about sex. Duh!” – Cal Bruns, marketing guru, Matchbox
Why this talk?

- Growing frustration with prevention failure
- Promoting prevention programmes with no evidence
- Bad science and rhetoric

Sex is God's joke on human beings. ~Bette Davis
“It’s like obesity. Behaviour change is impossible. Help them live with it.” – Prof Jeff Wing, endocrinologist
History of this talk

- Email arguments with prevention mob
- Behaviour change debate – World Bank
- NEJM article, Kenya talk
- 5th AIDS Conference, July 2011
- AJ Orenstein Lecture, follow up lecture Society, SANAC...
- The Zille discussion – opinion piece of HIV and incarceration
I sit in my HIV clinic with my frightened, bewildered patients who have to endure the headlines screaming for their punishment.

These people look pretty normal to me.
“If you can’t beat them, join them,” Zille wrote in her newsletter. “(Venter) seems to be finding the ultimate cop-out to avoid the debate on behaviour change and reinforcing denialism.”
Disclosures

• Support from Pepfar, pharmaceutical companies, Gates Foundation
• Clinician NOT behaviourist – PEP and patient experience
• TMI: Heterosexual, in a relationship>year
“We need better statistics for South Africa. And notification!”

Getting to Success: Improving HIV Prevention Efforts in South Africa

SOUTH AFRICA
HIV Epidemic, Response and Policy Synthesis
Caveats

• BAD data – poorly conducted studies, observational data, dubious conclusions
• ‘Common sense’ approach
• Sex data = nutritional data – recommendations with huge implications for lifestyle based on very poor research
• Relies largely on self-reported behaviours
• And non-verifiable ‘intended decision’
• No one really takes any account of data anyway – opinion upon opinion
Dutch study – men retracted their ‘only oral’ history

Keet et al., Orogenital sex and the transmission of HIV among homosexual men; AIDS 1992

- 102 homosexual men with known dates of seroconversion
- 20 reported no ano-genital sex behavior in prior 6-9 months on written questionnaires
- 11 of 20 (55%) later report receptive anal intercourse (RAI) in face-to-face interviews
- 5 of 9 (56%) who denied RAI had insertive anal intercourse
CDC 2007

- US: Average male population lifetime sexual partners = 7. Average female lifetime = 4
- Someone is lying
"The data shows that 31% of all deaths in 2011 were Aids-related. " - SA Institute of Race Relations
Before and after initiation of ARV therapy!
“...one of medicine’s modern miracles”
How long will people live for?

• ? 20 years or more on the treatment package !! Danish study – 39 years!
• American – lose 12 years
• French – NORMAL after 6 years
• Uganda 2011 study: Normalises life expectancy
• Geriatrics, fertility

Decades! ?normal life expectancy
Reality check...

• ½ all South Africans will contract HIV
• And will need treatment for life
We have to fix prevention!

For every 2 people started on ART

3 new infections

For every 2 people started on ART
So how does transmission work?
Multiple targets

Usually a single virus!

Cohen et al, NEJM, 2011
Cohen et al, NEJM, 2011
Figure 2. Natural History and Immunopathogenesis of HIV-1 Infection.

Cohen et al, NEJM, 2011
How does this help us?
### Infection Route

#### Sexual Transmission
- a. Female-to-male transmission: 1 in 700 to 1 in 3,000
- b. Male-to-female transmission: 1 in 200 to 1 in 2,000
- c. Male-to-male transmission: 1 in 10 to 1 in 1,600
- d. Fellatio: 0%

#### Parenteral Transmission
- a. Transfusion of infected blood: 95 in 100
- b. Needle sharing: 1 in 150
- c. Needle stick: 1 in 200
- d. Needle stick /AZT PEP: 1 in 10,000

#### Transmission from Mother to Infant
- a. Without AZT treatment: 1 in 4
- b. With AZT treatment: Less than 1 in 10

It is hard to get HIV!

*Adapted from Royce, Sena, Cates and Cohen, NEJM 336:1072-1078, 1997*
HIV ‘natural history’

Needs ARV’s

Gets HIV!

8 to 10 years
Sexual Transmission of HIV


**HIV RNA in Semen**
(Log$_{10}$ copies/ml)

**Risk of Transmission Reflects Genital Viral Burden**

1/30 - 1/200

1/1000 - 1/10,000

1/500 - 1/2000

1/100 - 1/1000

**Acute Infection**

3 wks

**Asymptomatic Infection**

**HIV Progression**

**AIDS**
HIV RNA in Semen
(Log_{10} copies/ml)

1/30 - 1/200
1/1000 - 1/10,000
1/500 - 1/2000
1/100 - 1/1000

Risk of Transmission Reflects Genital Viral Burden

1st 5/12: 50% of all transmissions!!!!!
(Wawer, 2005)

Sexual Transmission of HIV

Acute Infection 3 wks
Asymptomatic Infection
HIV Progression
AIDS
What is the biggest news of the year?

- HPTN 052
HPTN 052: Immediate vs Delayed ART in Serodiscordant Couples

HIV-infected, sexually active serodiscordant couples; CD4+ cell count of the infected partner: 350-550 cells/mm$^3$ (N = 1763 couples)

**Immediate ART**
Initiate ART at CD4+ cell count 350-550 cells/mm$^3$ (n = 886 couples)

**Delayed ART**
Initiate ART at CD4+ cell count ≤ 250 cells/mm$^3$* (n = 877 couples)

*Based on 2 consecutive values ≤ 250 cells/mm$^3$.

- Primary efficacy endpoint: virologically linked HIV transmission
- Primary clinical endpoints: WHO stage 4 events, pulmonary TB, severe bacterial infection and/or death
- Couples received intensive counseling on risk reduction and use of condoms

DSMB recommended release of results as soon as possible following April 28, 2011, review; follow-up continues but all HIV-infected partners offered ART after release of results

HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples

Total HIV-1 Transmission Events: 39
(4 in immediate arm and 35 in delayed arm; $P < .0001$)

Linked Transmissions: 28

+ Delayed Arm: 27

Immediate Arm: 1

Unlinked or TBD Transmissions: 11

Single transmission in patient in immediate ART arm believed to have occurred close to time therapy began and prior to HIV-1 RNA suppression

$P < .001$
HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples

Total HIV-1 Transmission Events: 39
(4 in immediate arm and 35 in delayed arm; \( P < .0001 \))

Linked Transmissions: 28

Delayed Arm: 27
Immediate Arm: 1

Unlinked or TBD Transmissions: 11

“Couples received intensive counseling on risk reduction and use of condoms”
Antiretroviral therapy for HIV prevention

Mathematical model of universal HIV testing annually with immediate ART for HIV+ in southern African epidemic

95% reduction in HIV incidence in 10 years

Prevalence <1% in medium term

Major reduction in mortality

Cost-saving in medium term
Is expanded HIV treatment preventing new infections?: Impact of antiretroviral therapy on sexual risk behaviors in the developing world

Kartik K Venkatesh\textsuperscript{a}, Timothy P Flanigan\textsuperscript{a} and Kenneth H Mayer\textsuperscript{b}

There have been dramatic increases in access to antiretroviral therapy (ART) across the developing world, and growing public health attention has focused on the possibility of utilizing ART as a means of slowing the global HIV epidemic. The preventive impact of ART will likely depend on decreasing levels of sexual risk behaviors following treatment initiation. The current review paper examines the impact of wider access to ART on sexual risk behaviors among HIV-infected individuals in the developing world. The observational studies to date demonstrate that ART is associated with a significant reduction in unprotected sex following treatment initiation. While data on the impact of ART on possible risk compensation is rapidly expanding across the developing world, more evidence is still needed before we can safely conclude expanded treatment will result in durable decreases in sexual risk behaviors.

© 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins

AIDS 2011, 25:000–000
Who is winning the biological prevention race?
Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART for prevention; HPTN 052, Africa, Asia, Americas</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td>PrEP for discordant couples; Partners PrEP, Uganda, Kenya</td>
<td>73 (49-85)</td>
</tr>
<tr>
<td>PrEP for heterosexual men and women; TDF2, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>54 (38-66)</td>
</tr>
<tr>
<td>PrEP for MSMs; iPrEX, Americas, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment; Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td>Microbicide; CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td>HIV vaccine; RV144, Thailand</td>
<td>31 (1-51)</td>
</tr>
</tbody>
</table>
But: Caprisa 004

HIV infection rates in the tenofovir and placebo gel groups: 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</td>
<td>47%</td>
<td>50%</td>
<td>47%</td>
<td>40%</td>
<td>39%</td>
</tr>
<tr>
<td>(p-value)</td>
<td>(0.009)</td>
<td>(0.007)</td>
<td>(0.004)</td>
<td>(0.013)</td>
<td>(0.017)</td>
</tr>
</tbody>
</table>

WTF? Despite condoms, counselling ....
Where is the behaviour change???
**Partners PrEP: Both PrEP Strategies Significantly Reduce HIV Acquisition**

<table>
<thead>
<tr>
<th>Primary Efficacy Outcome, mITT* Analysis</th>
<th>TDF (n = 1584)</th>
<th>TDF/FTC (n = 1579)</th>
<th>Placebo (n = 1584)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV acquisitions, n</td>
<td>18</td>
<td>13</td>
<td>47</td>
</tr>
<tr>
<td>HIV incidence/100 PY</td>
<td>0.74</td>
<td>0.53</td>
<td>1.92</td>
</tr>
<tr>
<td>Efficacy vs placebo, % (95% CI)</td>
<td>62 (34-78)</td>
<td>73 (49-85)</td>
<td>--</td>
</tr>
<tr>
<td>*P value</td>
<td>.0003</td>
<td>&lt; .0001</td>
<td>--</td>
</tr>
</tbody>
</table>

*mITT analysis includes HIV acquisitions not detected at enrollment.

- No difference in efficacy of TDF vs TDF/FTC in reducing HIV acquisition ($P = .18$)
- Both PrEP strategies associated with significant reduction in HIV transmission vs placebo in both men and women
  - TDF efficacy: 68% in women, 55% in men
  - TDF/FTC efficacy: 62% in women, 83% in men

Partners PrEP: Other Outcomes

- Rates of death, serious adverse events, laboratory events low and not significantly different between arms
  - Mild GI effects primarily during Mo 1
- No significant difference in pregnancy rates between treatment arms
- Reported unprotected sexual behavior decreased on study, with similar decline observed across arms
  - One third of participants in each arm reported sex outside relationship

Lets talk about **closeting**

• “Closeted and in the closet are metaphors used to describe lesbian, gay, bisexual, transgender, queer/questioning and intersex (LGBTQI) people who have not disclosed their sexual orientation or gender identity “ – Wikipedia

• Associated with high risk behaviour – and poorer outcomes (HIV, suicide, substance use)

• Is it beyond gay men?
So, how is prevention going?

- Not great...
GLOBALLY, NEW HIV INFECTIONS HAVE PEAKED
Figure 1. Modelled absolute numbers of PLHIV, annual new infections, AIDS-related deaths and total population, adults aged 15-49 years, South Africa (1990-2008)

Sources: Spectrum estimates and mid-year population estimates from www.statssa.gov.za

2 The ASSA 2008 model also has revised assumptions about mortality rates in untreated HIV-infected individuals prompted by studies showing higher survival rates in African adults than had previously been assumed (ASSA, 2011).
The effect of changes in condom usage and antiretroviral treatment coverage on human immunodeficiency virus incidence in South Africa: a model-based analysis

Leigh F. Johnson, Timothy B. Hallett, Thomas M. Rehle and Rob E. Dorrington

J. R. Soc. Interface published online 18 January 2012

• “...estimated a small reduction in incidence owing to antiretroviral treatment by 2008. Increased condom use therefore appears to be the most significant factor explaining the recent South African HIV incidence decline.”
2% population; 33% HIV infections
Have we been targeting the Most at risk groups?

<table>
<thead>
<tr>
<th>Who we are targeting for prevention?</th>
<th>MARP</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>African females 20-34</td>
</tr>
<tr>
<td>In school youth</td>
<td>African males 25-49</td>
</tr>
<tr>
<td>Out of school youth</td>
<td>People with disabilities</td>
</tr>
<tr>
<td>Pregnant mothers</td>
<td>People who are high-risk drinkers</td>
</tr>
<tr>
<td>Privately insured</td>
<td>Persons who use drugs for recreational purposes</td>
</tr>
<tr>
<td>Workplace</td>
<td>Men who have sex with men</td>
</tr>
<tr>
<td></td>
<td>Males 50 years and older</td>
</tr>
</tbody>
</table>
HIV Incidence by modes of transmission

Sources: Draft results from Know your Epidemic project
Buzzword: Behaviour change

• “We can’t afford NOT to do behaviour change”
Behaviour change?...

- Despite 14-fold increase in condom use between 1997 and 2004!
- Education spending in $billions
- What behaviours were tackled? ABCs... ‘be faithful’
Types of relationships

• Age discordance
• Sugar daddies
• Multiple partners
• Concurrency
Older partners

- Older partners associated with increased HIV risk
  (Pettifor, Rees 2005)

**BUT: Age difference often < developed countries**

- Role of Sugar Daddies?
  
  
  - ... (sugar daddy relationships) accounted for only 4% of partnerships.
In an effort to create a taboo against cross-generational sex, the KZN department of health has introduced a Sugar Daddy campaign that aims to discourage young women from trading sex for goods and money.”
Concurrency and Africa: What’s up?
Do multiple concurrent partnerships explain our epidemic?

Francois Venter
Deputy Executive Director, WRHI
(Wits Reproductive Health and HIV Research Institute)
Associate Professor, Department of Medicine
University of the Witwatersrand, Johannesburg, South Africa

May 2011

Thanks to: Daniel Halperin, David Stanton, Helen Rees, Warren Parker, WHO, for their slides
“Concurrent partners”

Reassessing HIV Prevention” [in Generalized Epidemics]  
Potts M, Halperin D, Kirby D, Swidler A, Klausner J, 
Marseille E, Hearst N, Wamai R, Kahn J, Walsh J.  

*Science*, May 9, 2008

“*The largest investments in HIV prevention* for generalized epidemics are being made into those interventions where evidence for large-scale impact is increasingly uncertain. Resources and attention need to be shifted to those approaches where the evidence of impact is greatest, *namely male circumcision and decreasing multiple concurrent partnerships* [and increasing access to FP].”

Early successes: Uganda and “zero grazing”
Thinking

• People see people dying of a scary wasting illness around them
• They see promiscuous behaviour
• And they change their behaviour
• Less concurrency
But:

- Long lag phase
- Identifying ‘promiscuous people’ difficult – sex hidden
- Does not present uniformly
- Does NOT present as an STD
Sexual network structure and the spread of HIV in Sub-Saharan Africa: evidence from Likoma Island, Malawi

Stéphane Helleringer and Hans-Peter Kohler

Fig. 5: largest connected component. N = 685. It comprises more than 65% of the population of the 7 villages surveyed.

- A fifth of population in exclusive dyadic relationships
- Two-thirds linked by single chain of infections over last 3 years
- Networks not linked by sex workers or other “high frequency transmitters”
- Linked by decentralized, complex, robust chains of sexual relationships
I will not share my partner

ngoba...likusasa ngelami
Casual sex is dangerous. HIV Kills.
His boyfriend isn’t into everything he’s into in bed. When he needs to spice it up, he calls James.

It’s called concurrency, and it’s spreading infection.
BUT (but!):

- Question 1: DOES concurrency indeed drive HIV spread?
- Question 2: Does concurrency explain the Sub-Saharan epidemic?
- Question 3: Assuming concurrency IS the driver, can we do anything about it?
• Question 1: DOES concurrency indeed drive HIV spread?
• Plausible
Lifetime number of sexual partners, selected countries, mid-1990s

**Uganda**
- 1994
- *(Rakai Sexnet study)*
- 18% HIV+
- Pct of men with 10+ partners: >20

**United States**
- 1994
- *(NHSLS study)*
- 1% HIV+
- Pct of men with 10+ partners: >40

**Thailand**
- 1993
- *(BRAIDS study)*
- 2% HIV+
- Pct of men with 10+ partners: >60
Reported number of sexual partners: comparison of data from four African longitudinal studies

J Todd,1 I Cremin,2 N McGrath,3,4 J-B Bwanika,5 A Wringe,5 M Marston,3 I Kasamba,1 P Mushati,6 T Lutalo,6 V Hosegood,3 B Žaba3

ABSTRACT

Objective: To compare reported numbers of sexual partners in Eastern and Southern Africa.

Methods: Sexual partnership data from four longitudinal population-based surveys (1998–2007) in Zimbabwe, Uganda and South Africa were aggregated and overall proportions reporting more than one lifetime sexual partner calculated. A lexis-style table was used to illustrate the average lifetime sexual partners by site, sex, age group and birth cohort. The male-to-female ratio of mean number of partnerships in the last 12 months was calculated by site and survey. For each single year of age, the proportion sexually active in a number of partners in the past 12 months with more than one partner in the calculated.

Results: Over 90% of men and 45% of age reported being in a single relationship with most reported partner. Overall, men reported higher sexual partners and partners in Uganda. The male-to-female ratio of mean number of partnerships in the last 12 months was 1.41 to 1.86. In the Masaka cohort, in south-western Uganda.

Conclusions: The longitudinal results show that reductions in the number of partnerships were more evident in southern Africa than in Uganda.

In the Masaka cohort in south-western Uganda.
Question 2: Does concurrency explain the Sub-Saharan epidemic?
• Subtext: Is African sexual behaviour different?
...A mathematical model “

“Results suggest that concurrent partnerships and other non-spousal partnerships are major drivers of the HIV/AIDS epidemic in South Africa. “
Concurrent Partnerships as a Driver of the HIV Epidemic in Sub-Saharan Africa? The Evidence is Limited

Mark N. Lurie · Samantha Rosenthal

The Concurrency Hypothesis in Sub-Saharan Africa: Convincing Empirical Evidence is Still Lacking. Response to Mah and Halperin, Epstein, and Morris

Mark N. Lurie · Samantha Rosenthal
Concurrent sexual partnerships do not explain the HIV epidemics in Africa: a systematic review of the evidence

Larry Sawers¹, Eileen Stillwaggon²


Concurrent partnerships and HIV: an inconvenient truth

Helen Epstein¹, Martina Morris²

Abstract
The strength of the evidence linking concurrency to HIV epidemic severity in southern and eastern Africa led the Joint United Nations Programme on HIV/AIDS and the Southern African Development Community in 2006 to conclude that high rates of concurrent sexual partnerships, combined with low rates of male circumcision and
Effect of concurrent sexual partnerships on rate of new HIV infections in a high-prevalence, rural South African population: a cohort study

Frank Tanser, Till Bärnighausen, Lauren Hurd, Geoffrey Garnett, Nuala McGrath, Marie-Louise Newell

Summary
Background Concurrent sexual partnerships are widely believed to be one of the main drivers of the HIV epidemic in sub-Saharan Africa. This view is supported by theoretical models predicting that increases in prevalence of concurrent partnerships could substantially increase the rate of spread of the disease. However, the effect of concurrent partnerships on HIV incidence has not been appropriately tested in a sub-Saharan African setting.

Methods For this population-based cohort study, in KwaZulu-Natal, South Africa, to try to find st

Figure 3. Community ranking according to HIV prevalence (A), HIV incidence (B) and transmission probability (C), Hlabisa sub-district, South Africa (2010)

Source: Bärnighausen et al. (2010)
KZN and the Africa Center

• Followed HIV negative women over 5 years
• “With respect to reported lifetime partners, a clear exposure-response relation was evident”
• “We find no evidence to suggest that concurrent partnerships are an important driver of HIV incidence in this typical high-prevalence rural African population. ... need for straightforward, unambiguous messages aimed at the reduction of multiple partnerships......”

Outside sexual partnerships and risk of HIV acquisition for HIV uninfected partners in African HIV serodiscordant partnerships.


- “A <5% reported sex with the infected partner and an outside partner in the same month”
- “HIV incidence was similar (2.87 vs. 3.02, p=0.7)”
Question 3: Assuming concurrency IS the driver, can we do anything about it?
we found no evidence of an impact of the intervention on our primary outcome measure: episodes of unprotected sex with non-wife partners in the preceding 6 months (median 5.4 episodes for men at intervention beer halls vs. 5.1 among controls, P = 0.98). There was also no evidence that the intervention reduced other risks for HIV.”

“Beer halls are venues in which male bonding, alcohol consumption and sexual risk taking are intertwined.”
“The findings suggest that the peer education program was not effective in reducing the age of sexual debut or condom use. Issues around the implementation of the program suggested that this was sub-optimal.”

Can Peer Education Make a Difference? Evaluation of a South African Adolescent Peer Education Program to Promote Sexual and Reproductive Health

Amanda J. Mason-Jones, Catherine Mathews and Alan J. Flisher

AIDS and Behavior
Volume 15, Number 8, 1605-1611, DOI: 10.1007/s10461-011-0012-1, August 2011
“My skepticism lies whether counseling interventions can change human behavior. Marketing can. Chaos, crisis, death, information can but I've not be convinced by 1:1 or group-level interventions with cute names.” – Dr Jeff Klausner, ex-CDC SA
And what if we’re wrong about concurrency?

- Intrusive, expensive, anxiety provoking
- Does NOT convincingly explain the SSA epidemic
- Need better quality data to make policy decisions
What about sex work?

- Illegal in SA, high levels of police harassment
- Challenge the two extremes views of sex work
- We ‘closet’ sex workers
Effective sex worker programmes?

- Education – often by peers
- Condoms and sexual health services
- HIV testing and counselling
- Supportive legal environment
What about the clients?

• Tijuana – sex work demographic
• Clients ‘closeted’
What about the gays?

- Men-who-have sex with men; the ‘down low’
- Transgenders
- “Silent” in Africa
### HIV Odds Ratios for MSM

<table>
<thead>
<tr>
<th>REGION</th>
<th>COUNTRIES</th>
<th>OR</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>15</td>
<td>33.3</td>
<td>32.3-34.2</td>
</tr>
<tr>
<td>Asia</td>
<td>7</td>
<td>18.7</td>
<td>17.7-19.7</td>
</tr>
<tr>
<td>Africa</td>
<td>4</td>
<td>3.8</td>
<td>3.3-4.3</td>
</tr>
</tbody>
</table>

Death penalty for gay transmission in Uganda debated

“...you are rotten. Same-sex is not acceptable” - Zulu King Goodwill Zwelithini, Jan 2012

Africa drives closeting! And it affects HIV control
Drug use?

• Needle exchange works
• Few successes internationally – Netherlands, Canada...
HIV PREVALENCE AMONG SW IN HAIPHONG, VIETNAM

Don't inject drugs

Do inject drugs

2

55
Drug use in SA?

• Intravenous use uncommon
• Other drugs vary
• Conventional debate: Hysteria and legislation
But!

- It’s not sex workers, MSM or drug users who drive the majority SA epidemic
Stop screwing around!

- “men have multiple partners”
- US: Up to 80% of one or both partners cheat in a stable relationship
- KZN: 1/3 men cheated over 5 years
- Shisana/HSRC: Married women higher risk than married men
Paternity testing...
Marriage protective?

• Data varies – married women high risk in some; marriage protective in others

• Tiger Woods, Bill Clinton, Angelina Jolie, Jacob Zuma, King Mwswati, Elizabeth Tailor...

• Hypocrisy of the American right (and left)
What about marriage? And lobola?

- Late marriage increases the likelihood of exposure to high life-time number of sexual partners, and concurrency

<table>
<thead>
<tr>
<th>Demographic characteristics (n=7006)</th>
<th>15-19</th>
<th>20-30</th>
<th>31-39</th>
<th>40-49</th>
<th>50-65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>98.5</td>
<td>82.4</td>
<td>49.2</td>
<td>34.7</td>
<td>37.7</td>
</tr>
<tr>
<td>Cohabiting with boyfriend/girlfriend</td>
<td>1.1</td>
<td>7.2</td>
<td>11.2</td>
<td>8.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Married</td>
<td>0.4</td>
<td>10.4</td>
<td>39.7</td>
<td>57.2</td>
<td>59.4</td>
</tr>
</tbody>
</table>

- Very low marriage rates in 20-30, very little cohabitation, low overall likelihood of marriage

Source: derived from Parker, W. presentation given 11 Dec. 2007; Setting a New Agenda for HIV Prevention; Johannesburg, SA.
Sex changes rapidly!

- **Oral sex internationally** - *Journal of Sexual Medicine* 2010: By ages 25-29, 8/9 women have performed fellatio, ½ done it in the past month. For men and cunnilingus, the numbers only slightly lower.

- **Anal sex in the US**
  - CDC 2007: 38.2% of men between 20 and 39; 32.6 percent of women ages 18 to 44 engage in heterosexual anal sex.
  - *Journal of Sexual Medicine* 2010: In 1992, the highest percentage of women in any age group who admitted to anal sex was 33. In 2002, it was 35. **Now it's 46%.**
  - Among women who had vaginal sex in their last encounter, the percentage who said they reached orgasm was 65. Among those who received oral sex, it was 81. But among those who had anal sex, it was 94. **Anal sex outscored cunnilingus.**

“Don't worry, it only seems kinky the first time.” ~Author Unknown
HIV and anal sex in SA

The prevalence of anal intercourse in this sample was 3.6% among both men and women. Sexually experienced youth accounted for 67% of the entire sample. Among sexually experienced youth, 5.5% of men and 5.3% of women reported ever engaging in anal intercourse. Only 0.06% of men reported other men as sexual partners; we therefore presume that we are describing heterosexual...
Networking and the internet

- Porn and the internet
- Allowed for rapid connections within small communities
- Facebook and MSM in Africa
- Grindr
- Porn link to LESS sexual violence
Behaviours change rapidly...

- **Mark Hunter** notes fundamental changes in late apartheid/post apartheid SA
- rising unemployment and social inequalities esp for poor women
- greatly reduced marital rates, increase of one person households
- rising levels of women’s migration, especially circular movements between rural areas and areas.
What if the biological transmission risk is SO high, that ABC doesn’t work?
“...Young people in the US report riskier sexual behaviors than young people in SA, despite the much higher prevalence of HIV infection in SA. Factors above and beyond sexual behavior likely play a key role in the ongoing transmission of HIV in South African youth,”
“There is a state of emergency among teenage girls in Southern Africa. Behavioral change campaigns have failed to demonstrate an effect on HIV incidence in heterosexual adolescents and will not likely have a large impact on adolescents in whom risky behaviors are not the primary problem.”

“This comparison of two nationally representative surveys of young people starkly underscores that behaviour is not the sole determinant of HIV risk.” Cait Hankins, UNAIDS
Immune activation is a dominant factor in the pathogenesis of African AIDS


First paper to show immune susceptibility in African AIDS
Human genes in HIV infection

Data from HIV natural history cohorts, candidate gene analyses & genome-wide studies have identified genes involved in HIV susceptibility:

1. innate & adaptive immunity (HLAs)
2. HIV dependency factors (CCR5)
3. intrinsic anti-virus factors (APOBEC)

Thanks to: Samantha Barichievy, CSIR
Genetic studies of African populations: an overview on disease susceptibility and response to vaccines and therapeutics

Giorgio Sirugo · Branwen J. Hennig · Adebowale A. Adeyemo · Alice Matimba · Melanie J. Newport · Muntaser E. Ibrahim · Kelli K. Ryckman · Alessandra Tacconelli · Renato Mariani-Costantini · Giuseppe Novelli · Himla Soodyall · Charles N. Rotimi · Raj S. Ramesar · Sarah A. Tishkoff · Scott M. Williams
“Considering biological causes for these racial disparities may help to destigmatize the issue and lead to new and more effective strategies for prevention."
Biological risks...

Host genes associated with HIV/AIDS: advances in gene discovery

Ping An and Cheryl A. Winkler
Laboratory of Genomic Diversity, NHLBI-Frederick, Inc., National Cancer Institute of Fr

Twenty-five years after the discovery of AIDS there is still no cure.

NIH Public Access Author Manuscript

This information is current as of February 8, 2011

REVIEW ARTICLE

Genetic determinants of HIV-1 infection and progression to AIDS: immune response genes

G. Kaur & N. Mehra
Department of Transplant Immunology and Immunogenetics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India

Proteases in MHC Class I Presentation and Cross-Presentation

Kenneth L. Rock, Diego J. Farfán-Arribas and Lianjun Shen

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doi:10.4049/jimmunol.0903399
http://www.jimmunol.org/content/184/1/9

Tissue Antigens ISSN 0001-2815

Genetic determinants of HIV-1 infection and progression to AIDS: immune response genes


Host genome influences on HIV-1 disease

Jacques Fellay
Center for Human Genome Variation Institute for Genome Sciences & Policy Duke University

Abstract

HIV host genetics seeks to describe as comprehensively as possible the impact of human genetic variation on the individual response to HIV-1 infection. Many associations between specific gene

Thanks to: Samantha Barichievy , CSIR
Viral differences?

• Max Essex, Chair of the Harvard AIDS Initiative – “about 30% of people acutely infected with HIV-1 Clade C maintain a high viral load for a much longer period than “
Biological Factors that May Contribute to Regional and Racial Disparities in HIV Prevalence

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Keywords
Africa, co-infections, HIV transmission, male circumcision, mucosal immunology, race

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Despite tremendous regional and subregional disparities in HIV prevalence around the world, epidemiology consistently demonstrates that black communities have been disproportionately affected by the pandemic. There are many reasons for this, and a narrow focus on socio-behavioural causes may be seen as laying blame on affected communities or individuals. HIV sexual transmission is very inefficient, and a number of biological factors are critical in determining whether an unprotected sexual exposure to HIV results in productive infection. This review will focus on ways in which biology, rather than behaviour, may contribute to regional and racial differences in HIV epidemic spread. Specific areas of focus are viral factors, host genetics, and the impact of co-infections and host immunology. Considering biological causes for these racial disparities may help to destigmatize the issue and lead to new and more effective strategies for prevention.
Highly efficient HIV transmission to young women in South Africa

Audrey E. Pettifor\textsuperscript{b,d}, Michael G. Hudgens\textsuperscript{c}, Brooke A. Levandowski\textsuperscript{b}, Helen V. Rees\textsuperscript{d} and Myron S. Cohen\textsuperscript{a,b}

Background: Young women in sub-Saharan Africa are at very high risk of HIV acquisition, and high prevalence levels have been observed among women reporting

Discussion

Our data indicate an incredibly high risk of HIV transmission per-partnership in young women in South Africa. These findings are supported by data from another large population-based study of young people in South Africa, which reported a per-partner HIV transmission probability estimate close to 1.0 for young women \cite{4}. Similarly, Glynn et al. \cite{3} concluded that the risk of HIV transmission at the first episode of sexual intercourse must be extremely efficient based on the high prevalence of infection observed among young women reporting one lifetime partner and few sexual contacts in Kisumu, Kenya. Taken together, these studies suggest that the probability of HIV acquisition among young women exposed to a single infected partner is extremely high.

• Of 3297 couples experiencing 86 linked HIV-1 transmissions, the unadjusted per-act risks of unprotected male-to-female (MTF) and female-to-male (FTM) transmission were 0.0019 (95% confidence interval [CI], .0010–.0037) and 0.0010 (95% CI, .00060–.0017), respectively.

Note: NOT ‘normal’ population
• Modifiable risk factors for HIV-1 transmission were plasma HIV-1 RNA level and condom use, and, in HIV-1–uninfected partners, herpes simplex virus 2 infection, genital ulcers, *Trichomonas vaginalis*, vaginitis or cervicitis, and male circumcision
"HIV-1 risk increased two-fold during pregnancy. Elevated risk of HIV-1 acquisition in pregnant women appeared in part to be explained by behavioral and other factors. This is the first study to show that pregnancy increased the risk of female-to-male HIV-1 transmission, which may reflect biological changes of pregnancy that could increase HIV-1 infectiousness"
Let's talk race...

Is it wrong to note 100m winners are always black?

The conclusions that are drawn from black athletes dominating the 100m final go a long way to explaining attitudes in wider society, argues Matthew Syed.
• “…black people are naturally better sprinters than white people. Indeed, it is an inference that seems obligatory, barring considerations of political correctness” BUT... Kenya
• “…not Kenya as a whole that usually wins these medals, but individuals from a tiny region in the Rift Valley called Nandi”
• - There is far more genetic variation within racial groups (around 85%) than there is between racial groups (just 15%)
• ‘car keys in the car park at night’ – we measure what we can measure (and race is easy!)
• Have we measured the right things?
To sum up

• We do NOT understand the relative contribution of behaviour vs biological factors to HIV risk
• Even within these categories, there is no agreement as to what is important – BUT there are definite biological risk factors (genes, physiological changes, co-factor infections, contraception etc etc)
• The ‘behaviours’ may be fluid and very complex – and difficult to intervene
• How can we then forge effective prevention programmes?
Conclusion (1)

• Treat HIV earlier, fix PMTCT, circumcise, contraception
• Re: Prevention and behaviour
• Historically: Sloppy epidemiology, inadequate science, sexual hypocrisy, common-sense wisdom
• BUT it is getting better – better data, critical thinking
Conclusion (2)

• Deal with drug use – decriminalise (SAMJ call)
• Sex workers and clients – why not ‘normalise’ the work?
• MSM – fight discrimination, encourage openness
Conclusion 3: The straight problem

• Should we talk about people in couples like we do about intravenous drug users?
• You or your partner is likely to be unfaithful – how can we make this safer?
• Get this out of the closet – ‘Monogamish’ – Dan Savage – a new way to deal with relationships
• The SA Kinsey report
Why we need a Kinsey report

• Sex: the thing that takes up the least amount of time and causes the most amount of trouble. ~John Barrymore
Choice quotes

• “Why can’t you single people just get married?”
• “These young girls are stupid”
• “Sex workers should be registered”
• “The epidemic should be allowed to take its course – THEN people would take responsibility”
• “Men have more partners than women”
• “Sugar daddies drive the epidemic”
• “Unbanning sex work/ gay men/ intravenous drug use will stop the epidemic”
• “If people would just return to a traditional family values based system…”
• “We need a moral revolution”
Could it be hormonal contraception?
Summary

- Hormonal contraception was associated with a 2-fold increase in risk of:
  - HIV-1 acquisition by women
  - HIV-1 transmission from women to men

- Increased HIV-1 risk was found among the subgroup using injectable methods
  - Risk was elevated among oral contraceptive users but the number of women using pills was small

- HIV-1 seropositive women using injectables had greater genital HIV-1 RNA levels which may be responsible for the increased rate of transmission to men
Table 2. Summary view of higher and lower HIV incidence rates

<table>
<thead>
<tr>
<th>Higher HIV incidence rate</th>
<th>Lower HIV incidence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Youth 15-24 years</td>
<td>Children 2-14, Adults 25+ years</td>
</tr>
<tr>
<td>African (black) people</td>
<td>Coloured, Indian, White people</td>
</tr>
<tr>
<td>Residence in urban informal areas</td>
<td>Residence in urban formal, rural formal and rural informal areas</td>
</tr>
<tr>
<td>Resident in KZN, GA and EC</td>
<td>Residents in the other provinces</td>
</tr>
<tr>
<td>Those sexually active but neither married nor cohabiting, and those widowed</td>
<td>Those married and those cohabiting</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Women not currently pregnant</td>
</tr>
<tr>
<td>People with low educational attainment</td>
<td>People with high educational attainment</td>
</tr>
<tr>
<td>People reporting more than one sexual partner (past 12 months)</td>
<td>People reporting one sexual partner (past 12 months)</td>
</tr>
<tr>
<td>Sex workers and their clients</td>
<td>General population</td>
</tr>
<tr>
<td>MSM</td>
<td>Individuals neither reporting paid sex nor male-to-male sex</td>
</tr>
</tbody>
</table>

Sources: Rehle et al., 2007 (BED assay on 2005 samples) and MoT report (UNAIDS HIV incidence model for 2010).
CDC 2007

• US: Average male population lifetime sexual partners = 7. Average female lifetime = 4
• Someone is lying
AFRICA MSM HIV PREVALENCE

- Senegal
- Mali
- Nigeria
- South Africa
- Egypt
- Sudan
- Kenya
- Tanzania
- Malawi
- Mauritania
- Ghana

- MSM
- General Population
Gaps in ‘behaviour change’ research

- Better behavioural research required - Is sex amenable to directive behaviour change interventions?
- Sort out the biology (acquisitional risk); also, link existing science to existing programmes
- Are the current public health people the right ones to do this? Use Coca Cola – people with a track record
- If this was a tablet... Why should we fund something that is poorly understood or measured, has little consensus or evidence for the intervention
- Better research (and less rhetoric and excuse making) needed!
The Reemerging HIV/AIDS Epidemic in Men Who Have Sex With Men

Harold W. Jaffe, MD, MA, FPPH
Ronald O. Valdiserri, MD, MPH
Kevin M. DeCock, MD, MPH, DTM&H

Since the first report of AIDS in 5 men who have sex with men (MSM) from Los Angeles,1 MSM have accounted for a higher proportion of AIDS cases than any other group in countries such as the United States (44%), Canada (65%), and Australia (64%).2,3 Although MSM first brought human immunodeficiency virus (HIV)/AIDS to the world's attention and, even in the absence of external funding, were the first to promote risk reduction strategies, prevention efforts for MSM appear to have faltered.

In this article, we examine current HIV/AIDS epidemiology in MSM, discuss why the epidemic may be re-emerging, and describe what can be done to address it. Although there is recognition and reporting of MSM with HIV/AIDS from low-income countries, the fear of acquiring this lethal new disease, Mann, who had already died, many more were sick, and no effective treatment existed. Both the gay media and leadership also actively promoted sexual risk reduction. Because little public funding for HIV prevention was available, the gay community relied on its own resources and developed an effective outreach to develop safe sex norms.

Trends in HIV/AIDS, Other Sexually Transmitted Infections, and Risk Behaviors in MSM

The number of MSM reported with HIV/AIDS is now increasing in many countries. The estimated number of cases of HIV/AIDS among MSM by year of diagnosis in the 33 states and US dependent areas with confidentially named-based HIV reporting increased from 1,167 in 2001 to 18,296 in 2005, a 13% increase.3 Thirteen Western European countries reported a 35% increase in HIV cases among MSM (from 3,180 in 1998 to 4,935 in 2005).

Although the sexual practices most likely to transmit HIV and other sexually transmitted infections are not always the same, the 10-fold increase in primary and secondary syphilis cases reported among MSM in the United States from 2001 to 2005 is a further indication of increasing frequency of unprotected sex.4

Recent US surveys of MSM document high rates of unsafe sex. Approximately 6,000 MSM participated in the National HIV Behavioral Surveillance System, which excluded men who knew they were infected with HIV.5 Of the more than 4,000 men who did not know the HIV infection status of their male

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