Sharing CAPRISA Experiences on FSW Cohorts around Durban, KZN: Improving Health Outcomes

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(On behalf of CAPRISA)

Research Seminar on Prostitution in SA: Developing a Research Agenda
Leriba Lodge, Pretoria 14 – 15 April 2010
Overview of CAPRISA Studies

**Epidemiology and Prevention**
- Focus: Young Women
- Seroincidence
- Microbicides
  - Vaccines
  - Behavioral

**Pathogenesis**
- Focus: Young Women
- Acute Infection
- TRAPS
- Chavi

**Treatment**
- Focus: Men and Women
- TB and HIV
- Treatment

CAPRISA’s HIV and TB Research and Treatment Agenda
Overview

- CAPRISA involvement with FSW related cohorts
- Discussing these cohorts and how they have informed CAPRISA research agenda
- Who are these women and where are they from
- Health issues
- Research participation
- Moving forward???
### Cohort
- 12 women selling beers and sex to truck drivers between Dec 1991 and May 1992

### Methods
- Cross-sectional
- Qualitative (10 in-depth interviews) and
- Quantitative (12 structured questionnaires) data collected
- Executed by a peer

### Demographic Data
- All Black, 17 to 34 years of age
- All single except for 1*married and 1* divorced
- 8 were mothers
- 2 from TVL and 10 from Natal
- Average school attendance of 5 years
- Sex work between 1 month and 8 years

### Sexual behavior per week
- 4 to 40 sex acts per woman (mean 22), and 2 to 10 per 24 hours
- Long and short sessions, truck station alternating with single sex hostels, but worked 7/7
- Refused oral and anal sex, and sex during menses.
### FSWs at a Major Truck Stop between DBN and JHB

**Abdoor Karim Q, Am J Public Health, 1995**

| HIV Related Issues | • Knowledge high (vs clients)  
| | • Condom usage infrequent despite access and availability |
| Reproductive Health Issues | • 58% not on contraception, 17% condoms, 17% IUD, and 8% oral contraception  
| | • 1* pregnant, continued with sex work  
| | • 58% intravaginal substance use e.g. Jik, Imbiza, Savlon, soap and water for contraception, cleansing and treatment, dry sex??  
| | • 50% STI previously – traditional and medical Rx |
| Male Behavior | • 58% had males who refused condom usage, 4 women agreed to have sex anyway  
| | • Aggressive/abusive if declined condom usage  
| | • Non payment if condom not used  
| | • Police demanding free sex and beer in return for not being jailed |
Epidemiology

From the original truck stop FSW work, we learned that:
1. Greatest risk for adverse health outcomes incl STIs and therefore in urgent and dire need for protective and preventive, and therapeutic health strategies
2. Where & how to access as a hard to reach marginalized group
3. How to improve participation and commitment to research
4. High HIV knowledge yet not translated into less risky behaviour

Pathogenesis:
Understanding pathogenesis (acute HIV events) at mucosal and systemic blood compartments is necessary for development of HIV preventive strategies such as vaccines and microbicides.

Prevention:
Serious issues with communication and negotiation of safer sex practices such as condom usage and therefore a male non-reliant strategy e.g. microbicide strategy might benefit them the most.
## Nonoxynol – 9 film Phase I Prevention Trial

**Rustomjee R, Abdool Karim Q, AIDS, 1999**

### Cohort
- A total of 20 FSWs at the same midway truck stop between JHB and DBN were enrolled.

### Methods
- 3-month cross-over acceptability and safety randomized double-blinded clinical trial.
- Eligibility: >18 years, at work for 3 months
- Daily dosing, 10 minutes before sex act
- Endpoints with regards to safety included the occurrence of lower genital tract symptoms, incident genital lesion and measurement of vaginal HIV RNA

### Demographic Data
- All Black, 19 to 43 years of age.

### Sexual behavior per week
- 5 to 30 sex acts per woman (mean 21)
- 6 to 20 clients (mean 9)

### Reproductive Health Issues
- 70% HIV seroprevalence ★
- STIs - 55% Syphilis★, 20% gonorrhoea, 19% genital lxs
- 80% Intravaginal substance use★
- 65% genital lesions on colposcopy in the active arm
HIV Distribution by Province among 15-49 Year Old Pregnant Women in 2008

Overall HIV Prevalence – FSW already 70%
CAPRISA FSW Associated Cohorts

- Acute HIV Infection Study
  - Phase I
    - CAP 002 = 193/245
  - Seroincidence Study
    - 050/051 = 13/594
  - Microbicide Trial
    - CAP 004 = 20/980
- CAP FSW = 226
Where did we Recruit from?

Challenging!!!

- Umbilo area, around Durban
- Clinical site within the Medical school
- Within a 45 km radius
- Truck stops, hot spots (harbor), street corners & hostels
- Word of mouth or visited by recruiters (CLO members)
Study Sites

Major Truck Stop enroute to JHB from DBN

CAPRISA Vulindlela Clinical Research Site, near Howick in KwaZulu-Natal

CAPRISA eThekwini Clinical Research Site in Durban
Study Sites

CAPRISA Vulindlela Clinical Research Site, Howick

CAPRISA eThekwini Clinical Research Site, Durban
CAPRISA Cohorts
CAP 050/051 Microbicide Preparedness Seroincidence Study Schema

**Purpose of study:** To determine the HIV incidence rates in potential cohorts for inclusion in the CAPRISA microbicide trial

**Design:** Observational prospective cohort

**Study size & population:** 542 sexually active women – family planning, VCT, and STI clinics, and FSW

**Eligibility:** Women between the ages of 14 and 35, serostatus negative for HIV and sexually active (having had sex in the preceding 3 months)

**Study duration:** February 2004 to May 2007

**Study Sites:** Ethekwini and Vulindlela. Ethekwini is in the Warwick triangle at the mouth of the city
Primary

Purpose of study: to determine the HIV incidence rates in potential cohorts for inclusion in the CAPRISA microbicide trial

Secondary

To assess the feasibility of establishing these cohorts at the Vulindlela and Ethekwini clinical research sites

To develop and describe the accrual process

To estimate rates of accrual and retention in an HIV-related research study among women targeted for the microbicide trial.
CAP 004 Phase IIB Tenofovir gel Microbicide Trial Schema

Purpose of study: Assess safety & effectiveness of the vaginal microbicide 1% tenofovir gel for the prevention of HIV infection in women in South Africa

Design: Phase IIB, two-arm, double-blind, randomized, placebo-controlled trial

Study size: 900 sexually active, HIV-uninfected women aged 18 to 40 yrs

Study duration: May 2007 and February 2010

Study population: Family planning clients, STI clinic clients, women with multiple concurrent partners

Product: 1% Tenofovir Gel Placebo: Universal HEC
Primary objective

Purpose of study: To assess the safety & effectiveness of the vaginal microbicide 1% tenofovir gel for the prevention of HIV infection in women in South Africa

Secondary objectives

To assess the impact, if any, of tenofovir gel on:

- tenofovir resistance in HIV seroconvertors in the trial
- viral load in women who become infected with HIV during the trial
- the incidence rate of deep epithelial disruption
- pregnancy rates and outcomes
Title: Viral Set Point and Clinical Progression in HIV-1 Subtype C Infection: The role of Immunological and Viral Factors during Acute and Early Infection

Study Population: 160 women at least 18 years of age and older

Eligibility: Self identified FSW or women reporting ≥ 3 sexual partners over the preceding 3 months prior to enrolment

Study duration: August 2004 to date

Study site: Medical school DDMRI and Ethekwini CDC

Main purpose: To describe the impact of the interaction of virological, genetic, and immunological factors on clinical course of disease in acute and chronic incl treatment stages
AI Objectives/Different Components

Host genetics
- Trim5 alpha
- APOBEC3G
- IL10 polymorphisms
- CCL3L1
- Genome wide associations

Host immunity
- Humoral immunity
- Innate immunity
- Cellular immunity
- Inflammatory markers eg. cytokines

Viral Diversity
- Full-length genome sequencing
- Epitope identification
- Escape mutations
- Dual infections

Reducing HIV acquisition and disease progression

New knowledge to inform HIV vaccine development and testing
Screening Eligibility and enrolment

Has the participant had sex with more than 3 different partners in the last 3 months prior to screening? .................................................

If no, participant is ineligible for study

Number of sexual partners in the last 3 months. A steady partner is one that you see most of the time, often over a period of time. A casual partner is one that you may see only occasionally or even only once [sex worker cohort - include only those who do not pay you for sex].

a. Steady □ □ □ □ □ Too many to remember □ Refused

b. Casual □ □ □ □ □ Too many to remember □ Refused

In the last week, how many clients did you have? □ □ □ □ □ Clients
Screening and enrolment between August 2004 and May 2005
775 screened, 245 (31%) eligible and enrolled
193/245 (78.8%) were self identified FSW
Phase I monthly visits over 24 months, last termination in May 2007
20/193 (10.4%) seroconverted to HIV and enrolled into phase II

HIV Prevalence was 59.6%, dropped from 83% to 17% over 9 months
# Summary of Findings

## Demographics - N = 193

<table>
<thead>
<tr>
<th>Description</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - Median (Range; IQR)</td>
<td>36 (18 – 58; 25 – 42)</td>
</tr>
<tr>
<td>Highest Level of Schooling - Median (IQR)</td>
<td>10 (8 – 11)</td>
</tr>
<tr>
<td>Marital Status % (n)</td>
<td></td>
</tr>
<tr>
<td>Single, no partner</td>
<td>6.7% (13)</td>
</tr>
<tr>
<td>Married or Stable partner</td>
<td>29.0% (56)</td>
</tr>
<tr>
<td>Many partners</td>
<td>64.3% (124)</td>
</tr>
<tr>
<td>Any dependents? YES % (n)</td>
<td>75.1% (145)</td>
</tr>
</tbody>
</table>

## Sexual Behaviour (only at phase I, N = 193)

<table>
<thead>
<tr>
<th>Description</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years in sex work - Median (Range; IQR)</td>
<td>3 (0 – 31; 1 – 8)</td>
</tr>
<tr>
<td>Age started sex work - Median (Range; IQR)</td>
<td>26 (9 – 20; 14 – 53)</td>
</tr>
<tr>
<td>Days per week sex work - Median (IQR)</td>
<td>3 (2 – 3)</td>
</tr>
<tr>
<td>Sites of work per year - Median (Range; IQR)</td>
<td>3 (1 – 7; 1 – 3)</td>
</tr>
<tr>
<td>Clients per day - Median (Range; IQR)</td>
<td>2 (1 – 10; 2 – 3)</td>
</tr>
<tr>
<td>Clients in last week - Median (Range; IQR)</td>
<td>2 (0 – 30; 1 – 3)</td>
</tr>
</tbody>
</table>
# Summary of Findings

## Sexual Behaviour (only at phase I, N = 193)

- **Number of condoms used during last week - Median (IQR)** 4 (1 – 8)
- **Short sessions per week - Median (IQR)** 3 (2 – 5)
- **Overnight stays per week - Median (IQR)** 1 (0 – 2)
- **Number of sex acts per overnight stay - Median (IQR)** 2 (0 – 3)
- **How often was a condom used with your clients during the last month? % (n)**
  - Never 18.7% (36)
  - Sometimes, less than half 18.1% (35)
  - Often, more than half 23.8% (46)
  - Always 38.9% (75)
  - No clients last month 0.5% (1)
- **Anal sex ever** 34.6%
- **Oral sex ever** 25.4%
There were 20 HIV infections in the 193 CSW women, who had contributed a total of 307.6 person years of follow-up. The HIV incidence in this group was 6.5% (95% CI 4.0 - 10.0).

There were 8 HIV infections in the 52 non-CSW women, who contributed a total of 81.5 person years of follow-up. The HIV incidence in this group was 9.8% (95% CI 4.2 - 19.4).

The difference between the two incidence rates is not statistically significant (p=0.3243).
Where is the Epidemic: Age & Gender Disparities in SA

15 to 24 year olds have a 4 to 7 fold increase in risk vs male of the same age:  Simon et al 2006
STIs

STIs over time

Prevalence (%)

HIV Negative

HIV Positive

N=20

PhI Enrol

Month 6

Month 12

Month 18

Month 24

PhII Enrol

Month 6

Month 12

Month 18

Month 24

HSV-2 Ab
B. vaginosis
T. vaginalis
N. gonorrhoea
M. genitalium
C. trachomatis
HSV-2 (PCR)
Syphilis
# Inflammatory Conditions associated with Increased Risk of HIV Acquisition in Women

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical ectopy</td>
<td>4.9</td>
<td>Plourde et al. (1994)</td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>6.3</td>
<td>Plourde et al. (1994)</td>
</tr>
<tr>
<td>Ulcerative genital infection</td>
<td>2.9–3.0</td>
<td>DeVicenzi (1994), Martin et al. (1998), Kiddugavu et al. (2003)</td>
</tr>
<tr>
<td>Specific diagnosis of</td>
<td>1.4–2.8</td>
<td>Martin et al. (1998), Kleinschmidt et al. (2007)</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal candidiasis</td>
<td>2–3.3</td>
<td>Kapiga et al. (1998), Martin et al. (1998)</td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>1.3–3.6</td>
<td>Laga et al. (1993), Martin et al. (1998)</td>
</tr>
<tr>
<td>Neisseria gonorrhoea</td>
<td>1.8–5.2</td>
<td>Laga et al. (1993), Kapiga et al. (1998), Martin et al. (1998), Kleinschmidt et al. (2007)</td>
</tr>
<tr>
<td>Herpes simplex virus-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(seroprevalent)</td>
<td>2.8–4.4</td>
<td>Baeten et al. (2007b), Brown et al. (2007)</td>
</tr>
<tr>
<td>(seroincident)</td>
<td>4.6–8.6</td>
<td>Brown et al. (2007)</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>1.6–5.8</td>
<td>Ungchusak et al. (1996), Martin et al. (1998)</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>1.2–4.8</td>
<td>Laga et al. (1993), Martin et al. (1998), Kleinschmidt et al. (2007)</td>
</tr>
</tbody>
</table>

Oskari Heikinheimo, Human Repro Update, 2009
Sexual Behaviour

- HIV Negative: N=193
- HIV Positive: N=20

- Ever had anal sex? YES
- Anal sex in the past month? YES
- Ever had oral sex? YES
- Oral sex in the past month? YES
- Use any substance to clean your vagina between/after sex? YES
Efficiency of Transmission

Table 1 | Probability of HIV-1 transmission

<table>
<thead>
<tr>
<th>Route</th>
<th>Probability per coital act</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male-to-male transmission</td>
<td>1/10–1/1,600</td>
</tr>
<tr>
<td>Male-to-female transmission</td>
<td>1/200–1/2,000</td>
</tr>
<tr>
<td>Female-to-male transmission</td>
<td>1/200–1/10,000</td>
</tr>
</tbody>
</table>

Anal Sex riskier than penovaginal sex
Anal Sex

In these cohorts, from no reported anal sex to high prevalences

As early as 1991 –, high acquisition in women

Initially believed to carry no risk and a safe alternative to penovaginal sex

Associated with:
- Non condom use
- Incidence STIs
- Forced sex
- More pay

Lazzarin A, 1991
Abdool Karim Q, 2003
Ferguson A, 2003
Schwandt M, 2006
Contraception and Pregnancy

More pregnancies among condom users vs no contraception
0% using traditional methods for contraception
Factors Associated with Increased Risk of HIV Acquisition in Women

Female-associated factors

Young age at coital debut (Pettifor et al., 2004) –
Age < 25 years (Laga et al., 1993; Morrison et al., 2007)
Age > 45 years (De Vincenzi, 1994)
≥ 4 sex partners (Kapiga et al., 1998)
Practice of anal sex (De Vincenzi, 1994)
Not living with partner (Morrison et al., 2007)

Partner/male-associated factors

Advanced stage of HIV infection (Saracco et al., 1993; DeVicenzi, 1994; Quinn et al., 2000)
High circulating HIV load (Quinn et al., 2000)
Uncircumcised partner (Kapiga et al., 1998)
Understanding Acute HIV Infection Events: Implications

Wong Justin, Horizon scientific press 2007

DeFranco, Locksley and Robertson (2007)

Risk of transmission

Health Issues

Sexual practices – HIV and STI
- Inconsistent condom use
- Intravaginal substance use (dry sex, cleanse, treat infections, contraception)
- Anal sex

Inconsistent contraception use
- Unplanned and unwanted pregnancy – TOP

Violence – rape, kidnap, physical
- Clients, peers, managers, police

Soft targets for drug dealers, human traffickers
Health Implications: Public Health

Need to understand risk factors for acquisition in order to develop strategies to prevent or reduce infections in this cohort e.g.
- Changing sexual behaviour
- Microbicides
- Male circumcision

Now need to go beyond this and understand issues around prevention of transmission:
- Commencing ARV’s in Acute Infection
- HSV-2 treatment/prophylaxis
- Test and treat

“Concentrated epidemic”

Timing is of the essence!!!
Research Participation Issues
Research Participation Challenges

Recruitment:
- High HIV prevalence
- Time constraints - work mostly at night
- Perceived stigmatization by research staff

Disclosure:
- Wary of sharing intimate and sensitive information for fear of victimization, prosecution and discrimination
- Tired and sleep deprived – poor concentration span

Retention:
- Highly mobile, poor retention in cohort studies and clinical trials
  - Change spots
  - Travel outside of the country with their clients
  - Change mobile numbers
  - Evade law
HIV negative CSWs
N=193

Completed Follow-up
N=141

Not enrolled into HEPS
N=44
- LTFU=1
- Ineligible=17
- Working=16
- Pregnant=5
- Relocated=5

Enrolled into HEPS
N=97

HIV+
N=20

Terminated prior to study completion
N=33
- Unable to contact=11
- Relocated=10
- Death=6
- Unable to adhere=4
- Refused participation=2

Active follow-up
N=12

Enrolled into HEPS
N=97

Initiated on ARV
N=7

Death
N=1

Retention:
 Consort Diagram

Not enrolled into HEPS
N=44
- LTFU=1
- Ineligible=17
- Working=16
- Pregnant=5
- Relocated=5

Enrolled into HEPS
N=97

Initiated on ARV
N=7

Death
N=1
## Retention Maintained Despite Rigorous Visit Schedule

<table>
<thead>
<tr>
<th>Month</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 2</td>
<td>Weekly and fortnightly (infection to end of month 3)</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Monthly (month 4 to month 12)</td>
</tr>
<tr>
<td>Phase 4</td>
<td>Quarterly (month 15 and beyond month 48)</td>
</tr>
<tr>
<td>Phase 5</td>
<td>Treatment (week 1, months 1, 3, 6 and monthly thereafter for a maximum of 5 years)</td>
</tr>
</tbody>
</table>
Developing a Research Agenda: Health Point of View

Women:

- Know health risky behaviors incl prevention thereof
- Constitutional rights (not applied) that protect them

**BUT**

- Risky behaviors continue to escalate as evidenced by high STIs incl. HIV, anal sex

**ISSUES:** ?? Male dominance and pressure, and poverty

- Research must be multi-pronged and focus also on males buying sex
Solution???

Women:

- Help them do what they do without predisposing themselves to greater health risks

  E.G.

- Improve working conditions e.g. institutionalise with rules and regulations and occupational health practitioners

Case Studies:
- Needle provision for IDU’s
- Condoms in brothels, Thailand

Intensify and prioritise prevention research agenda
Thank You for Your Attention
Questions and Comments
Acknowledgements

- **Acute Infection and HIV Pathogenesis Research:**
  - This research has been supported by the National Institute of Allergy and Infectious Disease (NIAID), National Institutes of Health (NIH) (grant# AI51794), the South African National Research Foundation (grant # 67385), the Columbia University-Southern African Fogarty AIDS International Training and Research Programme (AITRP) funded by the Fogarty International Center, NIH (grant # D43TW00231) and a training grant from LifeLab, a biotechnology centre of the South African Government Department of Science and Technology.

- **Microbicide Research**
  - The CAPRISA 004 Tenofovir gel trial is supported by the Centre for the AIDS Programme of Research in South Africa (CAPRISA), the United States Agency for International Development (USAID), Family Health International (FHI) (co operative agreement # GPO-A-00-05-00022-00, contract # 132119), and LIFElab, a biotechnology centre of the South African Government Department of Science and Technology. Support from CONRAD for the product manufacturing and packaging as well as support from Gilead Sciences for the Tenofovir used in the production of gel is gratefully acknowledged.

- **CAPRISA**
  - CAPRISA forms part of the Comprehensive International Program of Research on AIDS (CIPRA) funded by the National Institute of Allergy and Infectious Disease (NIAID), National Institutes of Health (NIH) and the US Department of Health and Human Services (DHHS) (grant# 1 U19 AI51794)

- **FOGARTY**
  - CU-SA Fogarty AIDS International Training and Research Program (grant # D43 TW00231);

- **ECOBIO/LIFELAB**

- **TB-HIV Treatment and Research:**
  - Financial support for CAPRISA from the National Institute of Allergy and Infectious Disease (NIAID), National Institutes of Health (NIH) (grant# AI51794) is gratefully acknowledged. The US President’s Emergency Plan for AIDS Relief (PEPFAR) funded the care of patients in the study. The Global Fund to fight AIDS, Tuberculosis and Malaria funded the drugs used in the study.