STI control as HIV prevention

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WHO, Geneva
Reproductive Tract Infections (RTI)

- Iatrogenic infections
  - e.g. post abortum

- Endogenous Infections
  - e.g. *Candida albicans* and *bacterial vaginosis*

- Sexually Transmitted Infections (STI)
  - e.g. gonorrhea, syphilis, herpes
Sexually Transmitted Infections

- Considerable morbidity
- High incidence and prevalence
- High rate of complications
- Bigger problem in women and young people
- Facilitate HIV transmission
STI: complications and sequelae

- PID
- Ectopic pregnancy
- Infertility (male, female)
- Perinatal, infant infections
- Genito-anal cancers
- AIDS
- Death
Burden of disease in adults 15-44 years in the developing world by sex, 1990

Maternal causes
- HIV
- STD
- Tuberculosis
- Respiratory infection
- Motor vehicle injuries
- Anaemia
- Depressive disorders
- Homicide and violence
- War
- Self inflicted injuries
- Alcohol dependence

Women
- 36%

Men
- 12%

Source: World development report 1993

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How STIs disseminate?

Basic Reproductive rate

$$R_0 = B \times c \times D$$

Transmission efficiency

Rate of sex partner change

Duration of infectiousness
How to control STIs?

Decreasing Reproductive rate!

\[ R_0 = B \times c \times D \]

- Barriers and vaccines
  - Enhance resistance
  - and reduce susceptibility

- Health promotion
  - Alter sexual behaviour

- Case and partner management
  - Shorten duration of infection

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STI: social and demographic determinants

- Socio-economic status (behaviour and health systems)
- M:F rates (migration, missing males)
- Age structure of the population
- Population density
STI transmission dynamics at population level

- General population
- Bridging population
- Core transmitters

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Sexually Transmitted Diseases

Symptomatic

Asymptomatic

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Global epidemiology
Estimated new cases of curable STI* among adults, 1999

- **North America** 14 million
- **Western Europe** 17 million
- **North Africa & Middle East** 10 million
- **Sub-Saharan Africa** 69 million
- **Latin America & The Caribbean** 38 million
- **Eastern Europe and Central Asia** 22 million
- **East Asia & Pacific** 18 million
- **South & South-East Asia** 151 million
- **Australasia** 1 million

Global total: 340 million

*gonorrhoea, chlamydial infection, syphilis and trichomoniasis*
Estimates

- Starting from reporting and correcting for underreporting
- Delfi method
- Starting from prevalence (our choice):

\[
Incidence = \frac{\text{Prevalence}}{\text{Duration of infection}}
\]
Prevalence and incidence of STIs may vary widely

- within countries and between countries in the same region
- between urban and rural population
- in similar population groups.
STI Prevalence

- Differences reflect social, cultural and economic factors and different access to care
- Higher in urban residents, unmarried and young adults
Estimated new cases of curable STI* among adults, 1998

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* gonorrhea, chlamydial infection, syphilis and trichomoniasis
**Global estimates of curable STI, 1999**

<table>
<thead>
<tr>
<th>STI</th>
<th>Incidence</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>0.41%</td>
<td>0.95%</td>
</tr>
<tr>
<td>Gonorrhoeae</td>
<td>2.09%</td>
<td>0.77%</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>3.04%</td>
<td>2.89%</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>5.76%</td>
<td>3.85%</td>
</tr>
</tbody>
</table>
Global estimates of curable STI, 1999

<table>
<thead>
<tr>
<th>STI</th>
<th>New cases (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>12</td>
</tr>
<tr>
<td>Gonorrhoeae</td>
<td>62</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>92</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>174</td>
</tr>
</tbody>
</table>
Syphilis 2000

- Prevalence of 1.3% in Morocco
- In USA declining rates since 1992
- Congenital syphilis still a problem among minorities
- Epidemic in Eastern Europe and NIS
- Increase in Mongolia
- In Asia and Pacific: High rates in Cambodia (4%), Papua New Guinea (3.5%) and South Pacific (8%)

In Africa prevalence form 2.5% to 17.4% in PW
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Chlamydia 2000

Europe, prevalence in PW, from 2.7% in Italy to 8% in Iceland

In Asia and Western Pacific, prevalence in PW, 5.7% in Thailand up to 17% in India, One study in a rural population in Papua New Guinea showed a prevalence rate of 26%

Africa, prevalence in PW: from 6% in Tanzania to 13% in Cape Verde,

The higher prevalence female adolescents (24.1%-27%),

Low prevalence and incidence rates in the Nordic countries, following a wide scale screening programmes in the 1970s

USA: most common notifiable infectious disease (3 million/year)

Latin America and Caribbean, prevalence rates from 1.9% amongst teenager in Chile, 2.1%, PW, in Brazil, and 12.2% attendees FP in Jamaica

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In Western Europe, a significant decline in gonorrhoea rates has been seen. Outbreaks and an increase in cases have been reported in London and Paris.

In USA, between 1981 and 1996 the incidence of gonorrhoea decreased by 71.3%. Rates amongst blacks were 35% higher.

In Western Europe: trends in the incidence of gonorrhoea showed a steady decline. However, in 1997 the number of new cases was 17% higher than in 1996. First increase since 1976!

Sweden: trends in the incidence of gonorrhoea showed a steady decline. However, in 1997 the number of new cases was 17% higher than in 1996. First increase since 1976!

An important increase in gonorrhoea rates has been seen in Eastern Europe, in the NIS.

In Africa, prevalence rates in OW: 3.1% in Central African Republic and 7.8% in South Africa.

In Africa, prevalence rates: 3.1% in Central African Republic and 7.8% in South Africa.

Western Pacific: prevalence rates for gonorrhoea (3% or greater) are found in Cambodia and Papua New Guinea.

Australia, notification of gonocccocal infection doubled since 1991.
The question is no longer whether STI detection and treatment should be an essential component of HIV prevention programs, but rather how this component should be implemented to have maximal impact on HIV incidence in specific populations.

*MMWR 1998; 47 (No. RR-12): 1-24*
STIs and HIV transmission

- STIs are cofactors in HIV transmission
- STIs control reduces HIV transmission
Epidemiological synergy established between HIV/STIs

- Biological evidence
- Seroconversion studies
- Intervention trials
Epidemiological synergy established between HIV/STIs

Biological evidence
STD-related correlates of increased HIV genital shedding

**Cervico-vaginal secretions**
- mucopurulent cervicitis
- cervical ulcer
- vaginal ulcer
- leucocytes →
- *N. gonorrhoea*
- *C. trachomatis*

**Semen**
- urethritis
- leucocytes →
- *N. gonorrhoea*
Association between presence of STD and cervico-vaginal shedding of HIV–1

<table>
<thead>
<tr>
<th>STD</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC</td>
<td>60%</td>
<td>20%</td>
</tr>
<tr>
<td>CT</td>
<td>50%</td>
<td>30%</td>
</tr>
<tr>
<td>Ulcer</td>
<td>70%</td>
<td>10%</td>
</tr>
<tr>
<td>TV</td>
<td>50%</td>
<td>30%</td>
</tr>
</tbody>
</table>

From Ghys et al., AIDS, 1997
Impact of HIV load in semen and blood in 4 patients receiving treatment for urethral discharge

From Atkins et al., British Medical Journal, 1996
Median concentration of HIV-1 RNA in semen among 104 men with and without urethritis in Malawi

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median Concentration (x 10^4 copies/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without urethritis</td>
<td>1.5</td>
</tr>
<tr>
<td>With urethritis</td>
<td>12.4</td>
</tr>
<tr>
<td>1 week after treatment</td>
<td>8.9</td>
</tr>
<tr>
<td>2 weeks after treatment</td>
<td>4.1</td>
</tr>
</tbody>
</table>

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Hypothetical model of impact of STD on HIV genital shedding in men

From ISSTDR, Seville 1997; M. Cohen, plenary presentation

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Epidemiological synergy established between HIV/STIs

Seroconversion studies
## Longitudinal studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>STD studied</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron et al.</td>
<td>Heterosexual men, (Kenya)</td>
<td>Genital ulcer (mainly chancroid)</td>
<td>4.7</td>
</tr>
<tr>
<td>Darrow et al.</td>
<td>Homosexual men (U.S.A)</td>
<td>Syphilis</td>
<td>1.5-2.2</td>
</tr>
<tr>
<td>Holmberg et al.</td>
<td>Homosexual men (U.S.A)</td>
<td>Herpes</td>
<td>4.4</td>
</tr>
<tr>
<td>Laga et al.</td>
<td>Heterosexual women (Zaire)</td>
<td>Gonorrhoea Chlamydia infection Trichomoniasis</td>
<td>3.5 3.2 2.7</td>
</tr>
<tr>
<td>Stamm et al.</td>
<td>Homosexual men (U.S.A)</td>
<td>Herpes Syphilis</td>
<td>3.3-8.5 8.4-8.5</td>
</tr>
</tbody>
</table>
Epidemiological synergy established between HIV/STIs

Intervention trials
The Mwanza intervention
The Mwanza intervention

- Randomised study to assess impact of improved STI case management in HIV incidence, in Mwanza region, Tanzania
Mechanism of the Mwanza intervention

- Training and supervision
- Drug supply
- Health education on care seeking
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HIV incidence over 2 years in intervention and control communities in the Mwanza trial

- Establishment of STD reference centre in Mwanza town
- Training of HCW in syndromic approach, health education and condom promotion
- Regular supply of effective STD drugs through a separate distribution system
- Regular supervisory visits to health centres
- Periodic visits to the villages by health educators to promote prompt attendance to health centres for symptomatic STD
## Cure rate of STD achieved by health services in Mwanza

<table>
<thead>
<tr>
<th>Aware of symptoms</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attends health centre</td>
<td>80%</td>
<td>30%</td>
</tr>
<tr>
<td>Diagnosed as STD</td>
<td>77%</td>
<td>(77%)</td>
</tr>
<tr>
<td>Correct treatment prescribed &amp; obtained</td>
<td>74%</td>
<td>20%</td>
</tr>
<tr>
<td>Compliant</td>
<td>83%</td>
<td>(83%)</td>
</tr>
<tr>
<td>Proportion of patients cured</td>
<td>38%</td>
<td>4%</td>
</tr>
</tbody>
</table>

From Buvé et al., 1998

*HIV/AIDS/STI Initiative*
HIV incidence over 2 years in intervention and control communities in the Mwanza trial

Overall reduction of HIV: 42%

From Grosskurth et al., Lancet, 1995
The Rakai Intervention
Objectives of Rakai Intervention

1. To determine if reductions in STD prevalence and incidence would result in decreased HIV transmission/acquisition;

2. To determine if reduction in STD incidence and prevalence could be achieved effectively by mass STD treatment (chose mass therapy because of lack of infrastructure in the Rakai area).
Elements of Rakai Intervention

• Home visits were conducted every 10 months
• Questionnaires and samples were the same for everyone (intervention and control group)
• Intervention group received Azithromycin, Ciprofloxacin and Metronidazole, regardless of symptoms
• The control arm was given Mebendazole (treatment for worms), iron and vitamins
Medication used for Mass treatment for intervention and control groups in Rakai.

Intervention clusters (n=7871)  Control clusters (n =7256)

Treatment provided:

- Azithromycin 1000mg
- Ciprofloxacin 250mg
- Metronidazole 2g

- Mebendazole 100mg
- Iron-folate tablet
- Low dose multi-vitamin
The Rakai Intervention: results

- Significant reduction in prevalence of Syphilis
- Significant reduction in prevalence and incidence of Trichomoniasis
- Borderline significant reductions in prevalence of Bacterial vaginosis
- No differences of HIV incidence in the intervention and control communities
Possible reasons for differences between Mwanza e Rakai - I

- Stage of the epidemics
  - The proportion of new HIV infections attributable to STIs may decline when the HIV epidemic matures

- Kind of prevalent STIs: proportion of treatable and non treatable STIs (specially HSV2 and Bacterial vaginosis)

- Differences in the interventions and in their effects
Possible reasons for differences between Mwanza e Rakai - II

- Mass treatment: reintroduction rate depends on coverage, mobility and migration. Limited treatment available between rounds
- Syndromic management provides continuous control between episodes
- Relative importance of symptomatic and asymptomatic STIs in HIV transmission
Improving quality of STD case management at primary care level remains priority!

- Demand from patients
- Scope for improvement is enormous in most countries
- “Know how” is available
- Is effective in reducing HIV incidence (cf. Mwanza trial)
- Enhances prevention efforts in the clinic setting
Operational model of the role of health services in STD case management

Population with STD
Aware and worried
Seeking care
Correct diagnosis
Correct treatment
Treatment completed
Cure
Operational model of the role of health services in STD case management

- Population with STD
- Aware and worried
- Seeking care
- Correct diagnosis
- Correct treatment
- Treatment completed
- Cure

- Promotion of health care seeking behaviour
- Improve quality of care
- Attitudes of personnel

HIV/AIDS/STI Initiative
Operational model of the role of health services in STD case management

Population with STD
Aware and worried
Seeking care
Correct diagnosis
Correct treatment
Treatment completed
Cure

- Syndromic approach
- Include STD drugs in essential list
- Prescribe single dose
- Counsel about compliance
Clinical Diagnosis Approach

Identify the STD causing symptoms based on clinical experience

- even experienced STD providers often misdiagnose STDs
- miss mixed infections
- difficult for surveillance
Etiologic Diagnosis Approach

*Identify the organism causing the symptoms with laboratory tests and microscopy*

- tests can be time consuming and expensive
e.g. cultures cost $12 - $40 & take up to six days

- even rapid tests (RPR) require equipment to obtain and separate venous blood

- dependent technician & lab accuracy
Syndromic Diagnosis Approach

Identify all possible STDs that could cause syndrome and give recommended treatment based on epidemiologic and laboratory data

- Immediate treatment
  - decrease transmission
  - decrease complications
- Can do syndrome surveillance

- Need to weigh the ability to treat as many infected as possible (sensitivity) with the risks of overtreatment (specificity)
- resistance & stigma
THE SUPPOSED TO … APPROACH

Oops! I was supposed to . . .
Patient complains of urethral discharge or dysuria

Take history and Examine. Milk urethra if necessary

Discharge confirmed?

- No
  - Ulcer(s) present?
    - No
      - Use appropriate flow chart
    - Yes
      - Educate and counsel
      - Promote and provide condoms
      - Depending on counselling capabilities offer HIV testing

- Yes
  - Treat for gonorrhoea and chlamydia
    - Educate
    - Counsel if needed
    - Promote and provide condoms
    - Depending on counselling capabilities offer HIV testing
    - Partner management
    - Advise to return in 7 days if symptoms persist
Persistent/ Recurrent Urethral Discharge in Men

NB.: This flowchart assumes effective therapy for Gonorrhoea and Chlamydia to have been received and taken by the patient prior to this consultation.

Patient complains of persistent/recurrent urethral discharge or dysuria

Take history and Examine. Milk urethra if necessary

Discharge confirmed?

Yes

- Reinfection or poor compliance

No

Ulcer(s) present?

Yes

Repeat urethral discharge treatment

No

- Treat for Trichomonas vaginalis
  - Educate
  - Counsel
  - Promote/provide condoms
  - Partner management
  - Return in 7 days

Improved?

Yes

- Educate and counsel
  - Promote and provide condoms
  - Depending on counselling capabilities offer HIV testing

No

Refer

No

- Educate and counsel
  - Promote and provide condoms
  - Depending on counselling capabilities offer HIV testing

Yes

Use appropriate flow chart
Genital ulcers

Patient complains of genital sore or ulcer

Take history and examine

Sore/Ulcer/Vesicle present?

No

Yes

Vesicles or small ulcers with history of recurrent vesicles?

No

Yes

Treat for syphilis and chancroid
- Educate
- Counsel on risk reduction
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing
- Partner management
- Advise to return in 7 days

Yes

Clinical deterioration, or no improvement after one week?

No

Yes

- Educate and counsel
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing

Yes

- Management of herpes
- Educate
- Counsel on risk reduction
- Promote and provide condoms
- Depending on counselling capabilities offer HIV testing

: Needs adaptation to local epidemiological situation
Operational model of the role of health services in STD case management

Population with STD

Aware and worried

Seeking care

Correct diagnosis

Correct treatment

Treatment completed

Cure

asymptomatic STD

- Partner notification
- Case finding
- Screening
- Selective mass treatment
What proportion of STD is asymptomatic?

**Incidence studies**
- 2% of incident infections with gonorrhoea remained asymptomatic for at least 2 weeks (Harrison *et al.*, New England Journal of Medicine, 1979)

**Prevalence studies**
- Screening pregnant women (GC/CT) 40%
- Screening FP clinic attenders (GC) 80%
- Male contact of clinical cases (GC) 29%
- Male contacts of cases detected through screening (GC) 76%
Where STD control is likely to have a maximum impact

- In settings with high prevalence of “relevant” STD (GUD, urethritis and cervicitis)
- Low quality of STD services
- At the earlier stages of the HIV epidemic

It is **NOT A MAGIC BULLET**, but an essential component of a package of multiple HIV prevention strategies.
WHO core functions in STI control

- Policy and advocacy
- Knowledge management
- Technical assistance to countries
- Partnerships development
- Norms and standards
- New technologies and tools development

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Strategic areas of action

- Improve access to quality STI care
- Promote early and effective health care seeking behaviour
- To establish simple and affordable surveillance systems to monitor trends and interrelations of HIV and STIs epidemics
Thank you
Danke
Merci
Grazias
Obrigado