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STIs in an International Setting

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Global prevalence of STIs
Adverse consequences of STIs and public health burden of disease
Strategies for STI control
STI control for HIV prevention
Section A

Prevalence and Public Health Burden of STIs
Main Curable STIs

- Syphilis
- Chancroid
- Gonorrhea
- Chlamydia
- Trichomonas
- Bacterial vaginosis (BV)—sexually associated rather than transmitted, treatable but recurrent
Estimates of Selected Curable Sexually Transmitted Infections

Global Total: 340 Million
Incidence of Syphilis: Estimates by Region
Incidence of Gonorrhea: Estimates by Region
Incidence of Genital Chlamydia: Estimates by Region

Data Are Probably Underestimates Due to the Relative Insensitivity of Most Diagnostic Tests Used
Chancroid (H. Ducreyi)

Estimated Incidence of Chancroid
Burden of Curable STIs

- Highest in developing countries
  - Lack of diagnosis and treatment
  - Low condom use
  - Early age of first intercourse
- Highest rates in Sub-Saharan Africa
- Largest number of cases in South and South-East Asia
- Highest burden of morbidity in women
Main Public Health Consequences of Curable STIs

- PID/infertility (gonorrhea, chlamydia, BV)
- Adverse pregnancy outcomes (syphilis, gonorrhea, BV, trichomonas)
  - Low birth weight, preterm birth, congenital infections
- Long-term morbidity (syphilis)
- Increased risk of HIV acquisition, mainly with ulcerative diseases (syphilis, H. ducreyi)
Morbidity Prevented by Treating 100 Women with Gonorrhea

(25 of Them Pregnant)

Cases

- PID
- Ectopic Pregnancy
- Infertility
- Ophthalmia Neonatorum

Cases Vs PID (25 of Them Pregnant)
Main Incurable Viral STIs

- HIV
- HSV-2 (herpes simplex type two)
- Human papilloma virus (HPV)
- Hepatitis B (mainly anal intercourse)
- HHV-8 (human herpes virus eight) cause of Kaposi’s sarcoma (mainly anal intercourse)
Prevalence of Incurable STIs

- HIV ~ 39 million
- HSV-2 prevalence, 10%-70%, depending on populations (highest in Africa)
- HPV almost all sexually active persons will be infected, especially in young
  - Most infections resolve (~18 months), but persistent infections can progress to cancer
  - Prevalence 25% - > 50%
Sequelae of Incurable STIs

- HIV—death, adverse pregnancy outcomes, mother-to-infant HIV transmission
- HSV-2—genital ulcer disease, cofactor for HIV, congenital infections
- HPV—cervical and anal cancers, genital warts, congenital laryngeal/pulmonary infections
Section B

Strategies for STI Control
Strategy for STI Control

- \( R_o = B \times C \times D \)

- \( R_o \) reproductive number or rate
  - \( R_o < 1 \) disease decreases, \( R_o > 1 \) disease increases, \( R_o = 1 \) steady state

- \( B \) transmission probability of infection per contact

- \( C \) number of infected contacts per unit of time

- \( D \) duration of infectiousness, can be reduced through treatment of curable STIs, or suppressive treatment of incurable STIs
Interventions attempt to do the following:

- Reduce exposure to an infected person by reducing partners and population STI prevalence—C (number of infected contacts per unit of time)
- Reduce the efficiency of transmission through barrier methods and safe sex—B (transmission probability of infection per contact)
- Reduce duration of infectiousness through treatment—D (duration of infectiveness)
Epidemio-Biological Model

Reduce Incidence

Reduce Duration

Symptomatic
- Health Seeking Behavior
- Improved STI Management

Asymptomatic
- Screening
- Partner Referral and Treatment
- Presumptive Treatment

Change Behavior
- Male/Female Barrier Methods
- Decrease Prevalence in “Core” and “Bridge” Groups
Symptomatic STIs

- Persons present for Rx
  - Need education to recognize symptoms
- Lack of diagnostic tests
  - Few cost-effective sensitive and specific tests currently available
- Treat syndromically
  - Discharge/dysuria—assume gonorrhea, chlamydia (i.e., urethral/cervical infections) or trichomonas or BV in women (vaginal infections)
  - Genital ulceration—assume syphilis, chancroid, or HSV-2
- Try to treat contacts
Most STIs are asymptomatic, especially in women
Most symptoms are non-specific (poor predictive value)
Discharge/dysuria in women is mainly due to vaginal infections (trichomonas, BV), but treated syndromically for cervical infections
  − Over treatment of cervical infections
  − Poor compliance with multi-dose/multi-day regimens
  − Selection of resistance (gonorrhea ++)
Most contacts remain untreated
Asymptomatic Infections in Women with Proven STIs

Rakai, Uganda

- Gonorrhea—66%
- Chlamydia—76%
- Trichomonas—80%
- BV—80%
Symptoms Have Poor Predictive Value in Persons with Proven STIs

- Proven gonorrhea among symptomatic individuals
  - Females—4.5% symptomatic
  - Males—25% symptomatic
- Proven trichomonas
  - Females—19.2% symptomatic
Genital Ulcers Mainly Not Due to Curable STIs

- Genital ulcer etiology
  - Syphilis—3.8%
  - Chancroid—2.5%
  - HSV-2—43.5%
  - Unknown—49.8%

- Only syphilis and chancroid curable
- HSV-2 can use suppressive therapy (e.g., acyclovir for seven days)
Operational Model of Syndromic Curable STI Case Management

- Syndromic management results in very low cure rates

- Population with STI: 100%
- Abnormal SX’s Recognized: ~55%
- Seeks and Obtains Care: ~38%
- Correct Diagnosis: ~28%
- Correct Treatment: ~17%
- Treatment Completed: ~9%
- Cured: ~5%
- Partner(s) Treated: ~1%
Policy Issues: Syndromic Management

- **Pros**
  - Allows treatment without diagnostic testing
  - Relatively inexpensive

- **Cons**
  - Small proportion of all curable STIs are symptomatic and present for treatment
  - Many symptomatic cases are not cured and contacts remain untreated
  - Most symptoms are non-specific or due to incurable STIs
  - Over treats cervical STIs
  - Does not interrupt transmission and provides poor STI control at population level
Pros
- Important to prevent transmission and re-infection

Cons
- Inconsistently implemented (11%–85%)
- Barriers to women notifying male partners (stigma, fear of violence)
- Men more likely to notify steady partners, but not casual partners
- Casual partners may be unknown
- Can be improved with education
- Cost-effectiveness unknown
Alternatives to Syndromic Management

- Screening of asymptomatic populations
  - Lack of low cost, sensitive and specific tests, not feasible in developing countries
  - Lack of non-invasive procedures
  - Syphilis testing in pregnancy modest success

- Mass or presumptive treatment
  - Treat whole populations, symptomatic, and asymptomatic
  - Use single dose, multi-drug (preferably oral), and directly observed therapy to assure cure and minimize resistance
  - Cover contacts
Section C

STI Control in Selected Populations
At Risk Populations

- Method of STI management depends on target population
- High risk “core groups”
  - Commercial sex workers (CSWs)
  - Clients
- Bridging populations
  - Clients of CSWs
- Vulnerable populations
  - Pregnant women
- General populations
STI Management in High Risk Groups

- Screening and treatment
  - Only successful where CSW are legal or are government supervised (e.g., Hamburg)

- Presumptive treatment
  - Cost-effective in high STI prevalence settings

- Condom promotion
  - Critical component of all prevention

- Control of sex trade (e.g., trafficking of women)
Presumptive STI Treatment of CSWs in South African Mines:

**Effects on STIs in CSWs and Their Clients**

STIs in CSWs and Miners, Following Presumptive Treatment of CSWs, SA (Steen STDs 2000)

Reduced Gonorrhea, chlamydia and GUD in CSWs and miners
Randomized Trial of Monthly Oral Azithromycin CSWs in Nairobi

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>4.7</td>
<td>12.7**</td>
</tr>
<tr>
<td>Chalmydia</td>
<td>6.3</td>
<td>14.5**</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>11.3</td>
<td>20.4**</td>
</tr>
</tbody>
</table>

Presumptive treatment successful in high risk groups
Policy Implications:

Presumptive Treatment of High Risk Groups

- **Pros**
  - Successful in research settings
  - Relatively low cost for high impact
  - Reduces STIs in clients who are bridging populations

- **Cons**
  - Not implemented programmatically
  - Requires access to CSW populations
  - Legal status of sex work, illegal immigration status, criminal control of sex work are obstacles
Promote consistent condom use to reduce the probability of infection per contact
Total STIs Reported and Condom Use Rates in Female Sex Workers in Thailand

100% Condom Campaign

YEAR

STDs (Thousands)

Condom Use Rates %

1987 1989 1991 1993 1995 1997 1999

0.00 50.00 100.00 150.00 200.00 250.00 300.00 350.00 400.00 450.00

0 10 20 30 40 50 60 70 80 90 100
### Consistency of Condom Use and STIs, Rakai

<table>
<thead>
<tr>
<th>STI and Consistency of Condom Use</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Syphilis Consistent Use</strong></td>
<td>0.7 (0.5-0.9)</td>
</tr>
<tr>
<td>Syphilis Inconsistent Use</td>
<td>1.1 (0.9-1.2)</td>
</tr>
<tr>
<td><strong>Gon/Chlam Consistent Use</strong></td>
<td>0.5 (0.3-0.9)</td>
</tr>
<tr>
<td>Gon/Chlam Inconsistent Use</td>
<td>1.4 (1.1-2.0)</td>
</tr>
<tr>
<td><strong>HIV Consistent Use</strong></td>
<td>0.4 (0.2-0.9)</td>
</tr>
<tr>
<td>HIV Inconsistent Use</td>
<td>1.0 (0.5-1.7)</td>
</tr>
</tbody>
</table>

- Only consistent condom use is protective
Consistency of Condom Use in Rakai

<table>
<thead>
<tr>
<th>Prevalence of Consistent and Inconsistent Use of Condoms</th>
<th>Consistent Condom Use %</th>
<th>Inconsistent Condom Use %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>4.4</td>
<td>16.5</td>
</tr>
<tr>
<td>1 Partner</td>
<td>4.4</td>
<td>10.0</td>
</tr>
<tr>
<td>2 Partners</td>
<td>4.9</td>
<td>39.5</td>
</tr>
<tr>
<td>3+ Partners</td>
<td>3.8</td>
<td>62.1</td>
</tr>
<tr>
<td>Never Married</td>
<td>16.3</td>
<td>28.6</td>
</tr>
<tr>
<td>Currently Married</td>
<td>0.7</td>
<td>13.7</td>
</tr>
</tbody>
</table>

Consistent condom use is low, particularly among the married. Inconsistent condom use increases with multiple partners.
Pros

- Only proven effective measure of STI and HIV control
- Cost-effective, especially with subsidized or free condoms

Cons

- Only consistent use is effective
- Most use is inconsistent
- Social and psychological barriers (e.g., use within marriage raises suspicion of infidelity)
- Acceptability—reduced satisfaction, condoms often stigmatized as methods for CSWs
Most women have at least one antenatal care (ANC) contact (>80% in most countries)

Screening pregnant women is a priority due to . . .
- Risks of STIs to fetus and newborn
- Accessibility to care
- Testing (RPR, TPPA) simple and cheap
- Treatment (IM penicillin, azithromycin), effective and cheap
Coverage of Syphilis Screening in Pregnancy Is Variable

<table>
<thead>
<tr>
<th></th>
<th>Nairobi %</th>
<th>Tanzania %</th>
<th>Rakai Uganda %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportions Screened</td>
<td>46</td>
<td>83</td>
<td>95</td>
</tr>
<tr>
<td>Prevalence of Syphilis</td>
<td>10</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Proportions Treated</td>
<td>25</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Pregnancy Outcome</td>
<td>Untreated Active Syphilis %</td>
<td>Treated Active Syphilis %</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>-----------------------------</td>
<td>---------------------------</td>
<td></td>
</tr>
<tr>
<td>Stillbirth</td>
<td>24.6</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Low Birth Weight</td>
<td>32.7</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>Preterm</td>
<td>20.0</td>
<td>8.5</td>
<td></td>
</tr>
</tbody>
</table>

Notes Available
Section D

STI Control in General Populations: Results of Three Community-Randomized Trials
Community-Randomized Trials of STI Control

- Three community-based trials in East Africa
  - Mwanza, Tanzania:
    - Syndromic management of STDs (Grosskurth (1995), et al., Lancet)
  - Rakai, Uganda:
  - Masaka, Uganda:
    - Syndromic management (Kamali, et al. (2003), Lancet)
- Pregnant women with syphilis were treated for ethical reasons
Community Randomized Trials of STD Control for HIV Prevention
### Rate Ratio (RR) of STIs in Treatment vs Control Arm of Randomized Trials

- Impact on STIs variable across trials

<table>
<thead>
<tr>
<th></th>
<th>Rakai RR (CI)</th>
<th>Masaka B RR (CI)</th>
<th>Mwanza RR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High titer syphilis</td>
<td>0.8 (0.7-0.9)</td>
<td>0.8 (0.5-1.0)</td>
<td>0.7 (0.5-0.9)</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>0.7</td>
<td>0.3 (0.1-0.6)</td>
<td>na</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>0.9</td>
<td>0.8</td>
<td>na</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>0.6 (0.4-0.9)</td>
<td>na</td>
<td>1.1 (0.9-1.3)</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td><strong>Mass Treatment</strong></td>
<td><strong>Syndromic + IEC</strong></td>
<td><strong>Syndromic</strong></td>
</tr>
</tbody>
</table>
Mass treatment more effective than syndromic management in reducing STIs
<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention (%)</th>
<th>Control (%)</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>3.4</td>
<td>3.3</td>
<td>1.04 (0.82 – 1.31)</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>4.7</td>
<td>15.9</td>
<td>0.28 (0.17 – 0.46)</td>
</tr>
<tr>
<td>BV</td>
<td>36.3</td>
<td>48.5</td>
<td>0.74 (0.66 – 0.84)</td>
</tr>
<tr>
<td>Gonorrhea/Chlamydia</td>
<td>1.9</td>
<td>4.3</td>
<td>0.42 (0.25 – 0.70)</td>
</tr>
<tr>
<td>Upper Genital Tract Infection</td>
<td>2.6</td>
<td>3.5</td>
<td>0.76 (0.53 – 1.10)</td>
</tr>
</tbody>
</table>

Presumptive Treatment and Maternal STDs Postpartum, Rakai

Notes Available
Mass treatment reduces maternal and infant STIs and adverse pregnancy outcomes

<table>
<thead>
<tr>
<th></th>
<th>Intervention (%)</th>
<th>Control (%)</th>
<th>Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular Gonorrhea</td>
<td>0.6</td>
<td>1.7</td>
<td>0.35 (0.18 – 0.67)</td>
</tr>
<tr>
<td>Ocular Chlamydia</td>
<td>0.6</td>
<td>1.1</td>
<td>0.44 (0.19 – 0.98)</td>
</tr>
<tr>
<td>Low Birth Weight</td>
<td>9.1</td>
<td>11.0</td>
<td>0.70 (0.51 – 0.96)</td>
</tr>
<tr>
<td>Preterm Birth</td>
<td>9.8</td>
<td>11.8</td>
<td>0.73 (0.54 – 0.99)</td>
</tr>
<tr>
<td>Neonatal Death/1000</td>
<td>25.4</td>
<td>29.1</td>
<td>0.83 (0.71 – 0.97)</td>
</tr>
</tbody>
</table>
Policy: Mass Treatment Advantages

- Covers asymptomatic infections
- No need for partner referral
- No need for diagnostic tests
- Cost effective if prevalence > 10%
- In pregnant women, reduces the prevalence of treatable STIs more effectively than syndromic management alone
Policy: Mass Treatment Disadvantages

- Logistical difficulty and costs
- Population access, acceptance, and adherence
- Reduced individual responsibility for health behaviors?
- Adverse drug reactions, resistance?
- Time limited—objective is to rapidly reduce STIs and then use standard methods
Hybrid of Mass Treatment and Syndromic Management

- \( R_0 = B \times C \times D \)
- Use mass treatment to rapidly reduce STI prevalence (i.e., C and D)
- Use syndromic management to maintain control of symptomatic STIs
- Use condom promotion (B) and risk reduction to reduce contacts (C)
Section E

STI Control for HIV Prevention
STI Control for HIV Prevention

- STIs are risk factors for HIV transmission and acquisition
  - Problem of confounding by sexual behaviors
- GUD (genital ulcer disease) breach mucosa and facilitate viral shedding or acquisition
- Inflammation recruits HIV target cells
- STIs (e.g., HSV-2) up-regulate HIV viral load, increasing infectivity
Can STI Control Reduce HIV Incidence?

- Three community randomized trials
  - Mwanza, Tanzania (Grosskurth (1995), *Lancet*)
  - Masaka, Uganda (Kamali (2003), *Lancet*)
- All treated curable STIs
  - Mwanza and Masaka used syndromic management
  - Rakai used mass, presumptive treatment
All trials showed reductions in treatable STIs
Only one showed an effect on HIV

<table>
<thead>
<tr>
<th></th>
<th>Rakai</th>
<th>Masaka A</th>
<th>Masaka B</th>
<th>Mwanza</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RR tmt/cont</td>
<td>0.97</td>
<td>0.94</td>
<td>1.00</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>(0.81–1.16)</td>
<td>(0.60-1.45)</td>
<td>(0.63-1.58)</td>
<td>(0.45-0.85)</td>
</tr>
</tbody>
</table>

Mass Treatment

Syndromic Management
Kenyan Trial of STD Control for HIV Prevention

in Commercial Sex Workers

- Monthly presumptive (mass) STD treatment with azithromycin
- Reduced STDs
- No effect on HIV (RR = 1.2, CI 0.6-2.5)
Marked reductions in maternal and infant STIs, no effect on HIV

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>RR(CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal HIV Incidence/100 py</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Incidence</td>
<td>3.4</td>
<td>2.3</td>
<td>1.41 (0.65-3.07)</td>
</tr>
<tr>
<td><strong>Mother-to-Child HIV Transmission (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postpartum</td>
<td>15.6</td>
<td>19.5</td>
<td>0.80 (0.4-1.6)</td>
</tr>
<tr>
<td>4-6 weeks PCR</td>
<td>25.0</td>
<td>29.6</td>
<td>0.84 (0.4-1.8)</td>
</tr>
</tbody>
</table>
Three out of four trials show no effect of treating curable STIs on HIV incidence

Attributable risk of HIV infection associated with curable STIs is low (< 20%)

Could incurable STIs be important?
- HSV-2 is a risk factor for HIV, causes GUD, increases HIV viral load and HIV shedding
- Ongoing trials of HSV-2 suppressive therapy for HIV control have started
Failure of STI control to prevent HIV is disappointing and has reduced donor interest in STI control

Need for innovative strategies (e.g., mass treatment and syndromic management)

Need for more aggressive control of viral STIs (e.g., HSV-2 using suppressive therapy)

Vaccines?
- HSV-2 vaccines are not effective
- HPV vaccines are highly effective in reducing infection and persistence
Your feedback on this lecture presentation is very important and will be used for future revisions. Please take a moment to evaluate this lecture. The Evaluation link is available on the lecture page.