Epidemiology of STIs in Developing Countries and STI-HIV Interactions

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Mabey D, Ndowa F, Latif A. What have we learned from STI research in sub-Saharan Africa? Sex Transm Inf 2010;86: 488-92
Curable STIs: WHO Estimates of Cases per Year

<table>
<thead>
<tr>
<th></th>
<th>1990s</th>
<th>2005</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhoea</td>
<td>62 million</td>
<td>94 million</td>
<td>78 million</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>92 million</td>
<td>101 million</td>
<td>131 million</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>174 million</td>
<td>250 million</td>
<td>142 million</td>
</tr>
<tr>
<td>Syphilis</td>
<td>12 million</td>
<td>11 million</td>
<td>6 million</td>
</tr>
<tr>
<td>Chancroid</td>
<td>6 million</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total new infections per year in 2012 estimated to be 357 million


Agents causing genital ulcer disease (GUD) in Africa before and after the 1990’s
Aetiology of Genital Ulceration in Zimbabwe (Mungati M et al. STD 2018: 45:61–68)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Harare n</th>
<th>Harare %</th>
<th>Bulawayo n</th>
<th>Bulawayo %</th>
<th>Beitbridge/Gatu n</th>
<th>Beitbridge/Gatu %</th>
<th>Total</th>
<th>%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>72</td>
<td>35%</td>
<td>54</td>
<td>42%</td>
<td>200</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HSV</td>
<td>17</td>
<td>23.6%</td>
<td>35</td>
<td>47.3%</td>
<td>46.3</td>
<td>77</td>
<td>38.5</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>T. pallidum</td>
<td>9</td>
<td>12.5%</td>
<td>13</td>
<td>17.6%</td>
<td>18.5</td>
<td>10</td>
<td>16.0</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>C. trachomatis</td>
<td>1</td>
<td>1.4%</td>
<td>0</td>
<td>0%</td>
<td>1</td>
<td>2</td>
<td>1.0</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>H. ducreyi</td>
<td>0</td>
<td>0%</td>
<td>0</td>
<td>0%</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>47</td>
<td>65.3%</td>
<td>28</td>
<td>37.8%</td>
<td>44.4</td>
<td>99</td>
<td>49.5</td>
<td></td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

NS indicates not significant. STD, sexually transmitted disease.
Trends in GUD pathogens in Johannesburg
Kularatne RS et al. PLoS One 2018

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Prevalence (95% CI)</th>
<th>N = 771</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes simplex virus</td>
<td>60.7% (57.2–64.1)</td>
<td>468</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>3.9% (2.7–5.5)</td>
<td>30</td>
</tr>
<tr>
<td>Chlamydia trachomatis L1-L3 (Lymphogranuloma venereum)</td>
<td>0.9% (0.4–1.9)</td>
<td>7</td>
</tr>
<tr>
<td>Haemophilus ducreyi</td>
<td>0.5% (0.2–1.4)</td>
<td>4</td>
</tr>
<tr>
<td>Klebsiella granulomatis</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>Mixed aetiology (HSV-2 + bacterial pathogen)</td>
<td>0.8% (0.4–1.7)</td>
<td>6</td>
</tr>
<tr>
<td>No STI pathogen</td>
<td>34.8% (31.5–38.2)</td>
<td>268</td>
</tr>
</tbody>
</table>

https://doi.org/10.1371/journal.pone.0194125.t003
Proportion of Genital Ulcers caused by *H. ducreyi* by Country and Year

** Estimated new cases of curable STIs per year (2012)**

Prevalence of STI and malaria among pregnant women in sub-Saharan Africa: a meta-analysis of 171 studies 1990-2011

Chico M et al. JAMA 2012; 307: 2079-86
The burden of congenital syphilis in sub-Saharan Africa

4-15% of pregnant women have syphilis (mean 8%)
2 million women with syphilis become pregnant each year
1,600,000 are not treated
492,000 infants die of syphilis


Incidence of gonorrhoea per 100,000 total population per annum

• Swaziland: 3,000

• Kampala, Uganda: 15,000

• England and Wales: 50
  – (Communicable Disease Report, 2000)
Common incurable STIs

- HIV: >3 million new cases in 2010
- *Herpes simplex* virus type 2 (HSV-2)
- Human papillomavirus (HPV) (cervical cancer)
- Hepatitis B virus

HSV-2 seroprevalence by age & sex in rural Mwanza, Tanzania

*Obasi A, et al. JID 1999; 179: 16-24*
Reasons for High Prevalence of STIs in Lower-Income Countries

- Demographic factors
- Urban drift
- Migrant labour
- Prostitution
- Polygamy, multiple (concurrent) partners
- Lack of medical facilities, training, supervision
- Lack of drugs
- Misuse of drugs, and antibiotic resistance
HIV and STDs: Epidemiological synergy

• HIV increases severity and duration of some STIs
• Some STIs facilitate transmission of HIV by increasing infectiousness of HIV + partner and/or susceptibility of HIV-

Fleming & Wasserheit. Sex Transm Inf 1999;75:3-17

Do STIs enhance HIV transmission?

1. Biological evidence (plausibility)
2. Epidemiological evidence
   – Cross sectional studies
   – Prospective studies
3. Conflicting evidence from intervention studies (RCTs)
4. Implications for control programmes
Mechanisms by which STIs may increase HIV transmission

<table>
<thead>
<tr>
<th></th>
<th>Infectiousness</th>
<th>Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal disruption</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Target cell recruitment &amp; activation</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Altered cytokine production</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Enhanced HIV replication</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Do STIs increase HIV shedding?
Median concentration of HIV-1 RNA in semen among 135 men with and without urethritis in Malawi


<table>
<thead>
<tr>
<th></th>
<th>Without urethritis</th>
<th>With urethritis</th>
<th>1 week</th>
<th>2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median copies/ml</td>
<td>1.5</td>
<td>12.4</td>
<td>8.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>

STIs associated with increased detection & concentration of HIV-1 shedding

_Johnson LF & Lewis DA. STD 2008;35:946-959_

- Meta-analysis of 39 studies evaluating impact of STIs on genital tract HIV-1 DNA or RNA (Jan 2008)

- Effect on HIV detection & genital viral load (GVL)

<table>
<thead>
<tr>
<th>STI</th>
<th># studies</th>
<th>OR (95% CI)</th>
<th>Increased GVL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethritis</td>
<td>3</td>
<td>3.1 (1.1-8.6)</td>
<td>✔️</td>
</tr>
<tr>
<td>Cervicitis</td>
<td>5</td>
<td>2.7 (1.4-5.2)</td>
<td>✔️</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>7</td>
<td>1.8 (1.2-2.7)</td>
<td>✔️</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>5</td>
<td>1.8 (1.1-3.1)</td>
<td>✔️</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>6</td>
<td>1.5 (0.9-2.6)</td>
<td>✔️</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>9</td>
<td>0.9 (0.7-1.3)</td>
<td>✔️</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>11</td>
<td>1.0 (0.7-1.5)</td>
<td>?</td>
</tr>
<tr>
<td>Genital ulcers</td>
<td>4</td>
<td>1.8 (0.8-3.8)</td>
<td>✔️</td>
</tr>
<tr>
<td>Syphilis</td>
<td>4</td>
<td>1.3 (0.9-1.9)</td>
<td>✔️</td>
</tr>
<tr>
<td>Herpes</td>
<td>6</td>
<td>1.3 (0.7-2.5)</td>
<td>✔️</td>
</tr>
</tbody>
</table>
### Epidemiological Evidence

1. **Cross-sectional studies**
   - Many show association between HIV and STDs
   - Confounding due to sexual behaviour
   - Cannot prove direction of causality

2. **Prospective studies**
   **Risk factors for HIV acquisition in 285 male STI patients in Nairobi**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Yes (%)</th>
<th>No (%)</th>
<th>Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular CSW contact</td>
<td>15%</td>
<td>6%</td>
<td>3.2</td>
</tr>
<tr>
<td>Uncircumcised</td>
<td>23%</td>
<td>3%</td>
<td>8.2</td>
</tr>
<tr>
<td>Genital ulcer</td>
<td>14%</td>
<td>2%</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Prospective seroconversion studies: Genital ulcers

<table>
<thead>
<tr>
<th></th>
<th>Circumcised</th>
<th>Uncircumcised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer</td>
<td>1/18</td>
<td>5/19</td>
</tr>
<tr>
<td>No ulcer</td>
<td>0/28</td>
<td>0/8</td>
</tr>
</tbody>
</table>

HIV seroconversion after acquiring an STI from a single contact with a female sex worker

*Cameron et al. Lancet 1989; 2: 403-7*

**Influence of Genital Ulceration**

HIV-1 transmission probability per sexual intercourse in sero-discordant couples in Rakai, Uganda


![Graph showing the influence of genital ulceration on HIV transmission probability](image)
**STI/HIV cofactor hypothesis:**
STI control reduces HIV transmission

- Does it work?
- How much does it reduce HIV transmission?
- Which is the most effective intervention strategy for a given population?

**Community-randomised Intervention Trials**

- Mwanza / Tanzania 1991 - 95
  *Grosskurth et al. Lancet 1995; 346: 530-6*
  *Wawer et al. Lancet 1999; 353: 525-35*
**Epidemiological Background**

<table>
<thead>
<tr>
<th></th>
<th>Rakai</th>
<th>Masaka</th>
<th>Mwanza</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV prevalence (%)</strong></td>
<td>16.5</td>
<td>12.1</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>Stable/ falling</td>
<td>Stable/ falling</td>
<td>Rising</td>
</tr>
<tr>
<td><strong>HIV incidence (/100py)</strong></td>
<td>1.5</td>
<td>1.1</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Intervention Characteristics**

**Mwanza** – Syndromic STD management

**Rakai** – Mass STD treatment at 10-monthly intervals

**Masaka Arm A** – Information, education & communication (IEC)

**Masaka Arm B** – IEC *plus* syndromic STD management
HIV incidence over 2 years in intervention and control communities in the Mwanza trial


Overall reduction of HIV = 38% (21% - 58%)
Conclusions from the Mwanza Trial

- Improved syndromic management in rural health facilities reduced HIV incidence by 38%
- Effect not due to changes in sexual behaviour
- Effect probably due to reduction in duration of symptomatic STIs

- Intervention was highly cost effective:
  - $250 per HIV infection prevented
  - $11 per DALY saved
  

Summary – Significant Reductions

<table>
<thead>
<tr>
<th></th>
<th>Rakai</th>
<th>Msk A</th>
<th>Msk B</th>
<th>Mwanza</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Inc.</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>38%</td>
</tr>
<tr>
<td>Syphilis Inc.</td>
<td></td>
<td>48%</td>
<td>(38%)</td>
<td></td>
</tr>
<tr>
<td>High Titre Syph</td>
<td>20%</td>
<td>42%</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Prev.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NG Prev.</td>
<td></td>
<td>72%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male urethritis</td>
<td></td>
<td></td>
<td></td>
<td>(49%)</td>
</tr>
<tr>
<td>TV Prev. (F)</td>
<td>41%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSV-2 Inc.</td>
<td></td>
<td>35%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Curable STIs More Common in Mwanza than Rakai/Masaka

Conclusions from community-randomised intervention trials

In Uganda (compared to Mwanza)

• Mature HIV epidemic with higher prevalence and falling incidence
• Most new HIV infections acquired from regular partners
• Lower rates of reported recent high risk behaviour
• Lower prevalence of curable STIs
• Higher proportion of genital ulcers due to HSV2

Individually Randomised Trial
Kaul et al. JAMA 2004; 291: 2555-62

- Double-blind RCT of monthly azithromycin (1G) vs placebo in HIV negative Nairobi sex workers
- Primary endpoint: HIV incidence
- Secondary endpoints: Incidence of infection with *N. gonorrhoeae, C. trachomatis, T. vaginalis, T. pallidum*, BV.
- Analysis of *Herpes simplex* type 2 (HSV-2) infection performed post hoc

RCT of azithromycin PPT in Nairobi CSWs
Kaul et al. JAMA 2004; 291: 2555-62

- 466 HIV-negative women enrolled
  - 230 received azithromycin 1G monthly
  - 236 received placebo
- 341 followed for at least 2 years or until HIV seroconversion
RCT of azithromycin PPT in Nairobi CSWs
Kaul et al. JAMA 2004; 291: 2555-62

- No difference in HIV incidence between treatment and placebo group: 19/473 person years in treatment group (4%) vs 16/485 in placebo group (3.2%); adjusted RR 1.2, 95% CI 0.6-2.5
- Incidence of *N. gonorrhoeae*, *C. trachomatis* and *T. vaginalis* significantly reduced in treatment group
  - N. g. Rate Ratio 0.46, 95% CI 0.31-0.68
  - C. t. Rate Ratio 0.38, 95% CI 0.26-0.57
  - T. v. Rate Ratio 0.56, 95% CI 0.40-0.78

RCT of azithromycin PPT in Nairobi CSWs
Kaul et al. JAMA 2004; 291: 2555-62

- Incident HIV infection was associated with preceding infection with *N. gonorrhoeae* and *C. trachomatis*, and with baseline HSV-2 seropositivity
  - Rate ratio for N. g 4.9 (95% CI 1.7-14.3)
  - Rate ratio for C. t. 3.0 (95% CI 1.1-8.9)
  - Rate ratio for HSV2 6.3 (95% CI 1.5-27.1)
Conclusions

• *N. gonorrhoeae, C. trachomatis* and *T. vaginalis* infection did not increase susceptibility to HIV infection in this high-risk female population.

• The results suggest that *N. gonorrhoeae* and *C. trachomatis* infection increased the infectiousness of HIV-positive male sexual partners by 3-5 fold.

• (but cannot rule out confounding: HIV-infected male partners may be more likely to be infected with N.g and/or C.t)

• HSV-2 infection increased susceptibility to HIV infection 6-fold in this population.

HSV-2 and HIV relationships

• HIV may alter clinical presentation of HSV-2.
• HIV may enhance HSV-2 transmission.
• HSV-2 may alter susceptibility to HIV.
• HSV-2 may increase transmission of HIV.
Agents causing genital ulcer disease (GUD) in Africa before and after the 1990’s

Before 1990
- Undetermined: 35%
- Donovanosis: 35%
- LGV: 10%
- Chancroid: 15%
- Syphilis: 8%
- HSV: 8%

After 1990
- Undetermined: 30%
- Donovanosis: 8%
- LGV: 10%
- Chancroid: 45%
**Herpes simplex virus type 2 seroprevalence in rural Mwanza**

![Graph showing seroprevalence by age and gender.](image)

*Obasi et al, JID 1999; 179: 16-24*

**Published studies of HSV-2 sero-prevalence in non-high-risk adult populations in Africa**

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benin</td>
<td>30%</td>
</tr>
<tr>
<td>Cameroon</td>
<td>51%</td>
</tr>
<tr>
<td>CAR</td>
<td>82%</td>
</tr>
<tr>
<td>Congo</td>
<td>71%</td>
</tr>
<tr>
<td>DR Congo</td>
<td>40%</td>
</tr>
<tr>
<td>Zambia</td>
<td>55%</td>
</tr>
<tr>
<td>South Africa</td>
<td>40-80%</td>
</tr>
<tr>
<td>Tanzania</td>
<td>67%</td>
</tr>
<tr>
<td>Uganda</td>
<td>68%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>40%</td>
</tr>
<tr>
<td>Kenya</td>
<td>68%</td>
</tr>
<tr>
<td>Rwanda</td>
<td>51%</td>
</tr>
<tr>
<td>Cameroon</td>
<td>51%</td>
</tr>
<tr>
<td>Congo</td>
<td>71%</td>
</tr>
<tr>
<td>DR Congo</td>
<td>40%</td>
</tr>
<tr>
<td>Zambia</td>
<td>55%</td>
</tr>
<tr>
<td>South Africa</td>
<td>40-80%</td>
</tr>
</tbody>
</table>
HSV2 as a risk factor for HIV seroconversion in Mwanza

- Case-control study nested in main cohort
  - 127 HIV seroconverters
  - 636 randomly selected HIV neg controls
- Increased risk of HIV seroconversion in those HSV2 seropositive at baseline, and those seroconverting for HSV2, in men and women


HSV2 as a risk factor for HIV seroconversion in women

- Adjusted OR for HSV2 positivity at baseline = 1.3 (95% CI 0.6-2.8)
- Adjusted OR for HSV2 seroconversion = 2.4 (95% CI 0.8-6.8)
- 22% of incident HIV infections can be attributed to HSV2

HSV2 as a risk factor for HIV seroconversion in men

- Adjusted OR for HSV2 positivity at baseline = 6.1 (95% CI 2.5-14.9)
- Adjusted OR for HSV2 seroconversion = 16.8 (95% CI 6.1-46.3)
- 74% of incident HIV infections can be attributed to HSV2


Prevalent HSV-2 strongly & consistently associated with HIV acquisition

- Meta-analysis of 25 cohort & nested case control studies adjusted for age & sexual behavior (2009)
- Summary estimates
  - Gen pop’n women (6 studies) 3.4 (2.4-4.8)
  - Gen pop’n men (11 studies) 2.8 (2.1-3.7)
  - CSW (8 studies) 1.5 (0.75-3.0)
  - MSM (5 studies) 1.6 (1.2-2.0)
- Impact of incident HSV-2 usually even stronger

Glynn JR, Biraro S, Weiss HA. AIDS 2009
HSV suppressive treatment to prevent HIV acquisition
Watson-Jones D et al. NEJM 2008;358:1560-71

• 821 high risk HIV-, HSV2+ Tanzanian women
• Randomised to acyclovir 400mg bd or placebo
• Followed up every 3 months for 12-30 months
• Adherence estimated by tablet count

HIV incidence
• 4.12 per 100 person years in placebo group
• 4.44 per 100 person years in acyclovir group
• Rate ratio 1.08, 95%CI 0.64 - 1.83
HSV suppressive treatment to prevent HIV acquisition
Watson-Jones D et al. NEJM 2008;358:1560-71

At least 90% adherence to treatment in
• 51% of person years on acyclovir
• 52% of person years on placebo

HIV incidence in those taking >90% of tablets
• Acyclovir 2.52 (1.3-5.0)
• Placebo 4.31 (2.6-7.2)
• Rate ratio 0.58 (0.25-1.38)
HSV suppressive treatment to prevent HIV acquisition


- Double blind RCT of acyclovir 400mg bd vs placebo
- HIV -, HSV2 + individuals (n=3172)
  - women in Africa
  - MSM in Peru and USA
- 85% of doses taken in both arms
- 85% follow up at 18 months
- Incidence of GU reduced by 47% in acyclovir arm
- No difference in HIV incidence (3.9 vs 3.3 per 100 person years)

HSV suppressive treatment to prevent HIV transmission: the “Partners in Prevention” study


- 3,408 HIV sero-discordant couples in Africa
- All HIV + partners also HSV2 +
- HIV+ partners randomised to acyclovir 400mg bd or placebo
- Acyclovir reduced incidence of GU by 73%, plasma VL by 0.25 log, and CD4 count decline to <200 by 17%
- No difference in HIV incidence in seronegative partners between arms
Improved STI management for HIV prevention: only the Mwanza trial showed efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>N</th>
<th>Measure of Effect (95% CI)</th>
<th>Measure of</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grosskurth 1995</td>
<td>Syndromic STI mgt</td>
<td>12537</td>
<td>0.58 (0.42, 0.79)</td>
<td>RR</td>
<td></td>
</tr>
<tr>
<td>Wawer 1999</td>
<td>Azithromycin, ciprofloxacin, metronidazole</td>
<td>12726</td>
<td>0.97 (0.81, 1.16)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Ghys 2001</td>
<td>Intensive STI mgt</td>
<td>542</td>
<td>0.70 (0.25, 2.10)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Kamali 2003</td>
<td>Syndromic STI mgt</td>
<td>13598</td>
<td>1.00 (0.63, 1.56)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Kaul 2004</td>
<td>Azithromycin</td>
<td>416</td>
<td>1.20 (0.60, 2.50)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Gregson 2007</td>
<td>Syndromic STI mgt</td>
<td>11980</td>
<td>1.27 (0.92, 1.75)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Watson-Jones 2007</td>
<td>Acyclovir supp'n</td>
<td>821</td>
<td>1.08 (0.64, 1.83)</td>
<td>IRR</td>
<td></td>
</tr>
<tr>
<td>Celum 2008</td>
<td>Acyclovir supp'n</td>
<td>1358</td>
<td>1.16 (0.83, 1.62)</td>
<td>HR</td>
<td></td>
</tr>
</tbody>
</table>

STI control for HIV prevention: Future research directions

- **Concept** – continues to be strongly supported by observational data
  - Complex reciprocal biological interactions increase susceptibility & infectiousness
  - Synergy b/w HIV & other pathogens in part *because* of common behavioral risks

- **Interventions:**
  - Often ineffective - no “magic bullet” in sight
  - Further research needed to understand biological mechanisms underlying interactions
Conclusions

STIs in HIV+ individuals enhance HIV transmission to HIV- partners

• Overwhelming epidemiological evidence
• Accumulating biological evidence for both ulcers and discharge

Conclusions

STIs in HIV- individuals may enhance HIV acquisition:

• Stronger evidence for ulcers
• Weaker evidence for discharges
Implications for HIV control

• STI control remains a vital element of HIV prevention, especially early in the epidemic and where treatable STIs are common
• New strategies are needed for treatment and prevention of HSV2