HIV: A global perspective on epidemiology, diagnosis and prevention

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Denver Health
University of Colorado
November 13, 2012
Outline

• Current epidemic and targets for prevention
• Diagnosis of HIV infection
• Individual behavioral approaches: Risk reduction
• Biomedical and structural interventions: Male circumcision, PrEP, TasP, PMTCT
Adults and children estimated to be living with HIV | 2009

- North America: 1.5 million [1.2 million – 2.0 million]
- Caribbean: 240,000 [220,000 – 270,000]
- Central & South America: 1.4 million [1.2 million – 1.6 million]
- Western & Central Europe: 820,000 [720,000 – 910,000]
- Eastern Europe & Central Asia: 1.4 million [1.3 million – 1.6 million]
- Middle East & North Africa: 460,000 [400,000 – 530,000]
- East Asia: 770,000 [560,000 – 1.0 million]
- South & South-East Asia: 4.1 million [3.7 million – 4.6 million]
- Sub-Saharan Africa: 22.5 million [20.9 million – 24.2 million]
- Oceania: 57,000 [50,000 – 64,000]

Total: 33.3 million [31.4 million – 35.3 million]
## Global HIV Epidemic, 2011

<table>
<thead>
<tr>
<th>Number of people living with HIV</th>
<th>Total</th>
<th>34.2 million [31.8 million–35.9 million]</th>
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<tr>
<td>Adults</td>
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<table>
<thead>
<tr>
<th>People newly infected with HIV in 2011</th>
<th>Total</th>
<th>2.5 million [2.2 million–2.8 million]</th>
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Fig. 1.1 Number of people with access to antiretroviral therapy and the number of people dying from AIDS-related causes, low- and middle-income countries, 2000-2010

- People receiving antiretroviral therapy
- People dying from AIDS-related causes
Number of people receiving ART in low- and middle-income countries, by region, 2002–2011

- North Africa and the Middle East
- Europe and Central Asia
- East, South and South-East Asia
- Latin America and the Caribbean
- Sub-Saharan Africa
ART coverage in low- and middle-income countries
Global prevention efforts: Positive results

• World-wide incidence has declined 19% between 1999 and 2009
• Incidence has declined >25% in 22 countries in sub-Saharan Africa
• Behavioral change is the most important factor accounting for these declines
• Drops in HIV incidence correlate with
  • increased condom usage
  • delayed sexual debut
  • reductions in multiple partnerships
ABCs of HIV Prevention

Avoiding AIDS as easy as... Abstain be faithful condomise

Botswana
HIV Prevention: UN AIDS 2010

- Prevent sexual transmission
- Prevent maternal death and MTCT
- Provide access to ART
- Prevent people with HIV from dying with TB
- Empowerment and access to care for MSM, sex workers, TG people
- Prevent HIV infection in IVDU

- Meet the needs of women and girls, stop sexual and gender based violence
- Enhance social protection for people living with HIV
- Empower young people to protect themselves from HIV
- Remove punitive laws, practices, policies, stigma, and discrimination

www.unaids.org, 2010
WHO HIV/AIDS Prevention Goals 2012

- 15 million people on antiretroviral therapy (ART) by 2015
- Earlier testing
- Earlier initiation of antiretroviral therapy
- Focus on retention in care
- Strategic use of ART
  - HIV+ partners in serodiscordant couples, pregnant women, target populations (SW, IDU, MSM)
Rapid HIV 1/2 Antibody Tests

Insert device, test develops in 20 minutes
Read results in 10-12 minutes
## Rapid HIV Tests

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (95% C.I.)</th>
<th>Specificity (95% C.I.)</th>
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<tbody>
<tr>
<td><strong>OraQuick Advance</strong></td>
<td></td>
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</tr>
<tr>
<td>- whole blood</td>
<td>99.6 (98.5 - 99.9)</td>
<td>100 (99.7-100)</td>
</tr>
<tr>
<td>- oral fluid</td>
<td>99.3 (98.4 - 99.7)</td>
<td>99.8 (99.6 – 99.9)</td>
</tr>
<tr>
<td>- plasma</td>
<td>99.6 (98.5 - 99.9)</td>
<td>99.9 (99.6 – 99.9)</td>
</tr>
<tr>
<td><strong>Uni-Gold Recombigen</strong></td>
<td></td>
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<tr>
<td>- whole blood</td>
<td>100 (99.5 – 100)</td>
<td>99.7 (99.0 – 100)</td>
</tr>
<tr>
<td>- serum/plasma</td>
<td>100 (99.5 – 100)</td>
<td>99.8 (99.3 – 100)</td>
</tr>
</tbody>
</table>

Branson, BM.  [www.cdc.gov](http://www.cdc.gov)
HIV Prevention
Interventions by knowledge of HIV status

HIV Testing and Counseling
Harm reduction and Education
Condons

Prevention for HIV -
• Medical Male Circumcision
• Topical PrEP
• Oral PrEP
• PEP
• Vaccine

Prevention for HIV +
• ART
• PMTCT

Cohn, D. 2011
Behavioral Strategies for Prevention

• Voluntary testing and counseling

• Risk Reduction
  – Condoms
  – Decreasing number of sexual partners
    • False security of “serial monogamy”
    • Dangers of concurrent partnerships
    • Occupational Hazards: sex workers, truck drivers, soldiers
  – Intimate partner violence: peer support
  – Harm reduction programs for IVDUs
    • Needle exchange, education, drug treatment

Rasch, V et al. Contraception, 2007
Wodak A, AIDS 2008
Percentage of women and men receiving an HIV test and results in the 12 months preceding the survey in countries with repeat population surveys, 2003–2008

Source: Demographic and Health Surveys

www.who.int, accessed 10/31/10
Comprehensive knowledge of HIV (2007-2008)
Women and men age 15-49

Source: Demographic and Health Surveys

www.who.int, accessed 10/31/10
Condom usage and HIV prevalence: Sex workers in Cambodia

- HIV prevalence among women working less than 1 year at brothel
- HIV prevalence among women working less than 2 years at brothel
- Percent of sex workers reporting condom use at last sex

Success in Thailand

Concomitant with decreased STIs, HIV prevalence declined in high risk groups and pregnant women

Source: Sentinel Serosurveillance, Division of Epidemiology, Ministry of Public Health.
Prevention of HIV in Women

• Sub-Saharan Africa: 57% of people living with HIV are women
  – Population study in Uganda:
    • Women>men risk of incident HIV infection
    • Men>women with sexual partners outside marriage
  – Risk of marriage: 2.0 infections per 100 person years
  – Never married individuals: 0.7 infections per 100 person years

www.cdc.gov
Mermin J. JAMA. 2008
Special Considerations: Trauma and Sexual Violence

• 6-46% of women experienced attempted or completed forced sex by an intimate partner

• Rwanda:
  – HIV+ pregnant women risk of IPV 2x that of HIV-
  – Risk for IPV in pregnancy associated with sexual abuse prior to 14 yrs of age
  – 150-200K women infected with HIV as a result of rape in 1994 genocide

HIV Prevention
Interventions by knowledge of HIV status

- HIV Testing and Counseling
  Harm reduction and Education
  Condoms

Prevention for HIV -
- Medical Male Circumcision
- Topical PrEP
- Oral PrEP
- PEP
- Vaccine

Prevention for HIV +
- ART
- PMTCT

Cohn, D. 2011
PMTCT: Perinatal HIV in the US

- Prior to 1994: transmission rates 20-25%
- Current transmission rates: <2%
- 6,000-7,000 HIV+ women deliver/year
  - Status of most are known by delivery
  - HAART recommended for all regardless of CD4
  - Elective cesarian section if VL>1000
  - 10-12% receive little or no prenatal care
- < 100 infants infected in 2009

www.unaids.org, 2011
PMTCT: Resource-Limited Settings

• Worldwide 2.2 million HIV+ women deliver/year

• 370,000 new infections in children each year
  – Most due to mother-to-child transmission
  – Transmission rates 25-40% without ARVs
  – With ARVs peri-partum transmission 8-10%
  – Transmission rates at 18-24 months 15-25%
  – Breastfeeding accounts for ⅓ to ⅔ transmissions
<table>
<thead>
<tr>
<th>Studies Shown to Prevent MTCT</th>
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<tbody>
<tr>
<td><strong>AP</strong></td>
</tr>
<tr>
<td>14 wks</td>
</tr>
<tr>
<td>PACTG 076</td>
</tr>
<tr>
<td>Thai (Harvard)</td>
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<td>Thai (Harvard)</td>
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<tr>
<td>Thai (Harvard)</td>
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<tr>
<td>IvC (ANRS), PETRA</td>
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<tr>
<td>Thai (CDC), IvC (CDC)</td>
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<tr>
<td>PETRA, 012, SAINT</td>
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<tr>
<td>NVAZ</td>
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Regimens:
AZT; AZT+3TC; single dose (SD) NVP; AZT + SD NVP
Post-partum HIV infection

• Increased morbidity and mortality with mixed feeding (formula or cow’s milk)
• Exclusive breast milk recommended for 1\textsuperscript{st} 6 months
• Post-natal infection occurs in 16% of all breastfeeding infants by 24 months
• PEPI trial, Malawi
  – Extended infant prophylaxis 14 weeks post-partum
  – Advantage lost by 9-15 months

Kumwenda et al., NEJM 2008
2010 WHO Guidelines: PMTCT

• Women who meet criteria for treatment
  – start ART: life-long therapy
  – CD4 <350 cells/μL
  – CD4 > 350 cells, symptomatic (WHO stage 3 or 4)

• Women who do not meet criteria for HAART
  – Twice daily AZT for mom and NVP for breastfeeding infant or NVP or AZT for 6 weeks
  – 3 drug ART through pregnancy and breastfeeding and infant prophy for 6 weeks
  – Start at 14 weeks
PMTCT transmission coverage in low and middle income countries, December 2008

<table>
<thead>
<tr>
<th>Geographical region</th>
<th>Reported number of pregnant women living with HIV receiving ARVs for PMTCT</th>
<th>Estimated number of pregnant women living with HIV needing ARVs for PMTCT</th>
<th>Prevention of mother-to-child transmission coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>576,800</td>
<td>1,280,000</td>
<td>45%</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>17,100</td>
<td>32,000</td>
<td>54%</td>
</tr>
<tr>
<td>East, South and South-East Asia</td>
<td>21,700</td>
<td>83,000</td>
<td>25%</td>
</tr>
<tr>
<td>Europe and Central Asia</td>
<td>13,600</td>
<td>13,400</td>
<td>94%</td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>&lt;200</td>
<td>13,400</td>
<td>1%</td>
</tr>
<tr>
<td>Total</td>
<td>628,400</td>
<td>1,400,000</td>
<td>45% [37–57%]</td>
</tr>
</tbody>
</table>
Figure 1.1
The virtual elimination of mother-to-child transmission of HIV is possible
Estimated New HIV infections among children 0-14:
Different scenarios for 25 countries

## Biomedical Prevention of HIV

<table>
<thead>
<tr>
<th>Study</th>
<th>Length of study (years)</th>
</tr>
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<tbody>
<tr>
<td>HIV vaccine [Thai RV144 (6)]</td>
<td>3.5</td>
</tr>
<tr>
<td>1% Tenofovir gel [CAPRISA 004 (4)]</td>
<td>2.5</td>
</tr>
<tr>
<td>TDF/FTC PrEP in MSM [iPrEx (5)]</td>
<td>1.2</td>
</tr>
<tr>
<td>Circumcision [Orange Farm, Rakai, Kisumu (7)]</td>
<td></td>
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<tr>
<td>Immediate ART for positive partners (HPTN052)</td>
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Male Circumcision (MC) as HIV Prevention

- Meta-analysis in SSA: aRR 0.42 (CI 0.34-0.54) for heterosexual acquisition of HIV in circumcised males
- No prevention of transmission from men to women
- Unclear if benefit in MSM
- Increased risk of transmission during healing

Weiss et al., AIDS 2000
Wawer et al, Lancet 2009
2006: Potential Impact of MC on HIV in Sub-Saharan Africa

• Modeling: over the next ten years in SSA, MC could avert:
  – 2.0 (1.1-3.8) million new HIV infections (men and women)
  – 0.3 (0.2-0.5) million deaths (men and women)

• In the ten years after, MC could avert:
  – 3.7 (1.9-7.5) million new HIV infections
  – 2.7 (1.5-5.3) million deaths

• 2006: Cost effectiveness in South Africa
  – Cost per HIV infection averted: $181
  – 3 circumcisions \( \rightarrow \) 1 averted HIV infection
Roll out of MC in 9 countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Number circumcised</th>
<th>Time period</th>
<th>Number of sites established</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOTSWANA</td>
<td>6 180</td>
<td>April 2009 – March 2010</td>
<td>35</td>
</tr>
<tr>
<td>KENYA</td>
<td>91 300 (90 000 in Nyanza alone)</td>
<td>2009 – June 2010</td>
<td></td>
</tr>
<tr>
<td>NAMIBIA</td>
<td>350</td>
<td>September 2009 – June 2010</td>
<td>3</td>
</tr>
<tr>
<td>RWANDA</td>
<td>542</td>
<td>October 2009 – April 2010</td>
<td>9</td>
</tr>
<tr>
<td>SWAZILAND</td>
<td>10 000</td>
<td>2008 – June 2010</td>
<td></td>
</tr>
<tr>
<td>UGANDA</td>
<td>5 340</td>
<td>October 2008 – March 2010</td>
<td></td>
</tr>
<tr>
<td>UNITED REPUBLIC OF TANZANIA</td>
<td>4 700</td>
<td>September 2009 – May 2010</td>
<td>3</td>
</tr>
<tr>
<td>ZAMBIA</td>
<td>9 906</td>
<td>January – June 2010</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>10 000</td>
<td>2009</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 179</td>
<td>2007 – 2008</td>
<td></td>
</tr>
<tr>
<td>ZIMBABWE</td>
<td>6 070</td>
<td>May 2009 – April 2010</td>
<td>5</td>
</tr>
</tbody>
</table>
MC: Attitudes and Behaviors

- 2008: Botswana, Namibia, Swaziland
  - Nearly half of men planned MC
  - 2/3 of men and women planned to have male children circumcised
  - Inaccurate beliefs/perceptions of MC
    - 9-15%: circumcised male fully protected from HIV
    - 20-26%: no HIV test needed before MC
    - 14-26%: circumcised HIV+ men cannot transmit HIV
    - 8-34%: OK for circumcised male to expect sex w/o condom

Behavioral Change and Risk after MC

- Multi-site qualitative study, Swaziland
- Positive behaviors following MC
  - More responsible attitudes towards safe sex
  - Reducing number of sexual partners
  - Easier condom usage
- Risky behaviors following MC
  - Expressed in a minority of interviews
  - Period of sexual experimentation
- HIV counseling through MC critical to views

Grund J et al. AIDS Care
DOI:10.1080/09540121.2011.596516
Thai HIV Vaccine Trial: ALVAC and AIDSVAX

- MITT: 31.2% efficacy
- Low-moderate risk population
- Duration of effect?
- Insight into host immune response
- Correlates of protection?

Modified Intention to Treat Analysis

Probability of HIV-1 infection (%)

Rerks-Ngarm et al., NEJM 2009;362:2209-20
Microbicides: female controlled chemical barrier

- **Nonoxynol-9**
  - HIV incidence: N-9 16% vs Placebo 12%
  - 3+ uses of N-9 per day increased HIV 1.8x

- **Cellulose sulfate: S. Africa, Benin, Uganda, India**
  - 1425 enrolled, stopped early 2007: HR 2.02 (p=0.05)
  - Final analysis: cellulose sulfate HR 1.61 (p=0.13)

- **Carraguard Phase III trial, South Africa**
  - HIV incidence 3.3 per 100 woman years in Carraguard group vs. 3.8 per 100 woman-years in placebo
  - No statistical difference

Van Damme, Lancet 2002
Van Damme, NEJM 2008
Skoler-Karpoff, Lancet 2008
CAPRISA: Topical 1% Tenofovir gel

- 39% reduction in HIV acquisition
- No increased adverse events
- No TDF resistance in seroconverters

Karim QA et al, Science 2010;329:1168
iPrEx: Tenofovir-Emtricitabine (TDF-FTC) pre-exposure prophylaxis in HIV-neg MSM

44% reduction in incidence of HIV infection

Grant, RM et al NEJM 2010; 363:2587
Fem-PrEP: TDF-FTC in women

- Tenofovir-emtricitabine vs. placebo in Kenya, South Africa, Tanzania
- 1951 women enrolled, 95% adherence reported
- Study stopped early (Feb 2011)
- Equal number of new HIV infections in TDF-FTC and placebo groups
- Prelim data presented at CROI 2012
  - Less than 50% of patients with new infections had detectable drug levels
  - Giving away/selling pills? Adherence?

Roehr B, BMJ 2011;342:d2613
Van Damme et al. Abstract #32LB CROI 2012
Partners PrEP: TDF vs TDF-FTC vs Placebo

Risk reduction of 67% and 75%, respectively

HPTN052: Early vs delayed ART for HIV-1 infection prevention

- HIV- infected individuals in stable serodiscordant couples randomized to early ART (CD4+ 350-550 cells/μL) vs delayed (CD4+ <250 cells/μL)
- Couples attended visits together, received risk reduction counseling, condoms
- Early ART: relative reduction 96% in linked HIV-1 transmissions
- Treatment as Prevention (TasP)

Model projections illustrating the potential impact on HIV incidence in South Africa of annual voluntary HIV testing and counselling and ART.
Challenges

• Programmatic expansion for TasP
• Resistance to ARVs used in PMTCT/PrEP
• How to supply PrEP when 50% of those with HIV infection and indication for treatment are not receiving treatment
• Long-term toxicities from PrEP
• Adherence to PrEP
• Vaccine development
• Evaluation of combination approaches
• Behavioral compensation?
Summary

• HIV testing is feasible in resource limited settings and is integral to prevention
• PMTCT is essential
• Circumcision is a viable method that should become an accepted part of prevention programs
• TasP and PrEP can dramatically decrease the HIV epidemic but require significant expansion of coverage
Summary

- Condoms, education, and risk reduction are integral parts of HIV prevention programs
  - Oversimplified “ABCs” may not adequately address needs of community
  - Identify peer education and support groups
  - Victims of sexual violence, marginalized populations: structural interventions

- Successful HIV prevention: Behavioral, Structural, and Biomedical Interventions
Acknowledgements

• Michelle Haas, MD
• David Cohn, MD
Global HIV Epidemic, 2009

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<tr>
<td></td>
<td>Women</td>
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<td>Children (&lt;15 years)</td>
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Victims of trauma, sexual violence

• Prophylactic treatment for STIs (syphilis, gonorrhea, chlamydia, chancroid, trichomonas)
• Consider post-exposure prophylaxis for HIV
  – No conclusive evidence regarding efficacy
  – PEP not widely available
  – Treatment with 2-3 ARVs for 28 days
• Hepatitis B vaccine within 14 days if possible
• Tetanus vaccination if tears, abrasions
HIV Prevention 2012
Interventions by knowledge of HIV status

HIV Testing and Counseling
Harm reduction and Education
Condoms

Role of home testing?

Prevention for HIV -
• Medical Male Circumcision
• Topical PrEP
• Oral PrEP
• PEP
• Vaccine

Prevention for HIV +
• ART
• PMTCT

Cohn, D. 2011
Prevention: Key Populations

- Children and orphans
- Men who have sex with men
- Women and girls
- Indigenous people
- Migrant workers
- Prison settings
- People living with HIV
- Refugees and IDPs
- Rural communities
- Sex workers
- IV drug users
- Uniformed services
- Young people
- Educators and workforce

www.unaids.org, 2010