Updates – HIV/AIDS, 2009

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HIV/AIDS Department
World Health Organization
Updates

• Epidemiology and program scale-up

• Science and challenges in HIV prevention

• Evolution in HIV/AIDS treatment

• Conclusions
"…in the words of Scripture, the time has come to set aside childish things....."

"We will restore science to its rightful place and wield technology's wonders to raise health care's quality..."

Inaugural address, 20 January 2009
Global estimates for adults and children, 2007

- **People living with HIV**
  33 million
  [30 – 36 million]

- **New HIV infections in 2007**
  2.7 million
  [2.2 – 3.2 million]

- **Deaths due to AIDS in 2007**
  2.0 million
  [1.8 – 2.3 million]
HIV prevalence rates in adults by region, 2007

- Caribbean
- East Asia
- Eastern Europe
- Latin America
- North Africa and Middle East
- Northern America
- Oceania
- South and Southeast Asia
- Sub-Saharan Africa
- Western Europe

Percent infected

World average
HIV Incidence by modes of transmission

- Kenya: (76,315) new infections
- Zambia: (74,263) new infections
- Uganda: (91,546) new infections
- Mozambique: (118,279) new infections
- Swaziland: (11,381) new infections
- Lesotho: (23,269) new infections

### Sources
- Draft results from Know your Epidemic project
HIV prevalence in MSM in Africa

Almost 90% of HIV in pregnant women is found in 20 countries

Source: WHO, Towards universal access progress report 2008
HIV Incidence in Pregnancy and Post-Partum, Botswana – Implications for PMTCT

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV incidence:</td>
<td>1.3/100py</td>
<td>1.8/100py</td>
</tr>
<tr>
<td>Transmission rate</td>
<td>73%</td>
<td>36%</td>
</tr>
<tr>
<td>Attributable fraction for MTC</td>
<td>26%</td>
<td>17%</td>
</tr>
</tbody>
</table>

(Lu et al; CROI 2009: abs 91)
Survival of vertically infected children

Source: Ferrand et al, 2009
WHO revised HIV/TB estimates for 2007

- Evidence that prior HIV/TB estimates were too low
- 1.37 m. estimated incident HIV+ TB cases in 2007
- 26% estimated TB deaths in 2007 had HIV (456,000/1.77m)
- 23% of estimated HIV deaths in 2007 had TB (456,000/2m)
Global distribution of estimated HIV-positive tuberculosis cases
Trends in incident and prevalent HIV infections in adults, by region

Incident (new) infections

Prevalent (current) infections

Bongaarts J et al, 2008
Number of people receiving antiretroviral therapy in low- and middle-income countries, 2002-2007
Universal Access

My number one priority for UNAIDS is to go all out and to give my best energy to contribute to achieving our global commitments to universal access to comprehensive interventions for HIV prevention, treatment, care and support.

Michel Sidibé
## Global HIV prevention and treatment, 2007

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>On ART</td>
<td>3 million</td>
</tr>
<tr>
<td>Need ART</td>
<td>6.7 million</td>
</tr>
<tr>
<td>HIV-infected, asymptomatic</td>
<td>&gt;23 million</td>
</tr>
<tr>
<td>Annual HIV incidence</td>
<td>2.7 million</td>
</tr>
<tr>
<td>Accessed ART in 2007</td>
<td>1 million</td>
</tr>
</tbody>
</table>
Why has HIV prevention lagged behind?

• Limited number of evidence-based interventions
• Efficacy of behavioral interventions limited
• No simple biomedical interventions
• Interventions not brought to scale
• Inadequate targeting and monitoring
• Inadequate support for positive prevention
• Insufficient funding and political will

Adapted from Mermin J
Combination prevention
Multiple disciplines and approaches

- Biomedical Interventions
- Structural Interventions
- Community Interventions
- HIV testing and linkage to care
- Individual and small group behavioral interventions

Adapted from Coates, T
Provider-Initiated HIV Testing and Counseling in All Epidemic Types

HIV testing and counselling should be recommended to:

- Symptomatic patients
- HIV-exposed children or children born to HIV+ women
- Men seeking male circumcision for HIV prevention
Knowledge of HIV infection and behavior

After people become aware they are HIV-positive, high-risk sexual behavior is reduced substantially:

- United States – reduction in unprotected anal or vaginal intercourse with HIV-negative partners (HIV-pos Aware vs HIV-pos Unaware) 68%
  

- Uganda – HIV-infected persons who knew serostatus 3x more likely to use condom at last sex
  
New approaches to HIV testing

- Provider-initiated testing in health care settings
- Partner and family testing
- Mobile and community testing
- Door-to-door testing
**Completed efficacy trials of biomedical interventions for sexual transmission of HIV, 2009**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Completed</th>
<th>Efficacious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male circumcision</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>STI treatment</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>HSV-2 suppression</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Cervical barriers</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Microbicides</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>HIV vaccines</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>26</strong></td>
<td><strong>4</strong></td>
</tr>
</tbody>
</table>

Adapted from: Cohen J, Science 2008
HPTN 035 - Efficacy of vaginal microbicide PRO-2000 for HIV prevention in women

HIV incidence/100 p-y

<table>
<thead>
<tr>
<th></th>
<th>PRO 2000</th>
<th>Placebo</th>
<th>Buffer Gel</th>
<th>No Gel</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV incidence</td>
<td>2.7</td>
<td>3.9</td>
<td>4.1</td>
<td>4.0</td>
</tr>
<tr>
<td>(CI 95%)</td>
<td>1.9 - 3.7</td>
<td>2.9 - 5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard Ratio</td>
<td>0.70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0.46-1.08)</td>
<td>p=0.10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

30% reduction

Source: 16th CROI 2009, Montreal, Canada, 48 LB, Salim S. Abdool Karim et al
HPTN 035 - Efficacy of vaginal microbicide PRO-2000 for HIV prevention in women

<table>
<thead>
<tr>
<th></th>
<th>Incidence/100py PRO 2000</th>
<th>Incidence/100py Placebo</th>
<th>% HIV Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>High gel - Low condom</td>
<td>1.0 (3/299)</td>
<td>4.6 (15/324)</td>
<td>78%</td>
</tr>
</tbody>
</table>

Condom & gel use stratified by median
(Low < 85% and High ≥ 85%)

Source: 16th CROI 2009, Montreal, Canada, 48 LB, Salim S. Abdool Karim et al
Both TDF and TDF/FTC gel provided protection against repeated intravaginal challenge

16th CROI 2009, Montreal, Canada, Dobard C et al. Abs. 46

<table>
<thead>
<tr>
<th></th>
<th># animals</th>
<th># infected</th>
<th># protected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control: No gel</td>
<td>2</td>
<td>2</td>
<td>1 of 11</td>
</tr>
<tr>
<td>Control: Placebo gel</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>TDF gel</td>
<td>6</td>
<td>0</td>
<td>12 of 12</td>
</tr>
<tr>
<td>TDF/FTC gel</td>
<td>6</td>
<td>0</td>
<td>12</td>
</tr>
</tbody>
</table>

Low levels TDF (detected 60%, median 22 ng/mL) & FTC (detected 95%, median 67 ng/mL) in plasma at time challenge

P=0.005 compared to controls
Antiretroviral therapy for HIV prevention

- Transmission occurs only from HIV+ persons
- Viral load is strongest risk factor for transmission
- ART can lower viral load to undetectable levels
- PMTCT offers proof of concept of reduced transmission with ART
- Discordant couple studies are supportive

**Discordant Couple Studies**
- Reynolds S et al. 16th CROI, Montreal, Feb 2009 Abs. 52a
  - Rakai, Uganda
    - Incidence not on ART: 8.6/100 py
    - Incidence on ART: 0/25 py
  - Rwanda, Zambia
    - Incidence not on ART: 3.4/100 py
    - Incidence on ART: 0.7/100 py

- Marcelin A et al. 16th CROI, Montreal, Feb 2009 Abs. 51
Antiretroviral therapy for HIV prevention

• Mathematical model of universal HIV testing annually with immediate ART for HIV+ in southern African epidemic

• 95% reduction in HIV incidence in 10 years

• Prevalence <1% in medium term

• Major reduction in mortality

• Cost-saving in medium term

Preparing for now and for what's to come
Key Populations

- Adults, adolescents
- Children
- Pregnant women
- Women who may become pregnant
- TB patients
- Hepatitis B and C
- Injecting drug users

Criteria for Guidance

- Evidence
- Risks and benefits
- Cost and feasibility
- Acceptability

Priority Questions

- How to diagnose early
- How to monitor
- When to start
- What first line
- What second line

Critical Outcomes

- Mortality
- Disease progression
- Toxicity
- Retention on ART
- *(Reduction HIV transmission)*
Mortality Rates (deaths/100PYs) Stratified by Updated CD4 Counts

Lawn S et al.  CROI 2009, abs 140
TB Incidence Rates Stratified by Updated CD4 Cell Counts

(Poster #788)

Lawn S et al. CROI 2009, abs 788
Immediate vs deferred ART in acute OIs – ACTG A 15645

Zolopa et al, PLOS Medicine, 2009
Integrated ART/TB therapy vs sequential – South Africa

Kaplan-Meier survival curve: SAPiT trial

Survival

Integrated Arm
Sequential Arm

Months Post-Randomization

Intensive Phase of TB treatment
Continuation Phase of TB treatment
Post-TB Treatment

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

Salim Abdool Karim; CROI 2009: abs 36a.
### Key characteristics of current US, European and WHO ART guidelines

<table>
<thead>
<tr>
<th>Guidelines (year of publication)</th>
<th>When to Start in asymptomatic patients (preferred approach)</th>
<th>Preferred initial ARV therapy</th>
<th>Preferred subsequent ARV therapy</th>
<th>Preferred treatment failure/switching criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DHHS (2008)</strong></td>
<td><strong>CD4 &lt;350</strong> (stronger if &lt; 200)</td>
<td>2NRTI (TDF/FTC) + NNRTI (EFV) or bPI (ATV/r or DRV/r or FPV/r or LPV/r)</td>
<td>Guided by resistance testing/tropism testing</td>
<td>VL + CD4 (no consensus on thresholds)</td>
</tr>
<tr>
<td><strong>IAS (2008)</strong></td>
<td><strong>CD4 &lt; 350</strong> (consider if &gt; 350 in some situations)</td>
<td>2NRTI (ABC/3TC or TDF/FTC) + NNRTI (EFV) or bPI (ATV/r or DRV/r or FPV/r or LPV/r or SQV/r)</td>
<td>Guided by resistance/tropism testing</td>
<td>VL &gt; 500-1000</td>
</tr>
<tr>
<td><strong>EACS (2008)</strong></td>
<td><strong>CD4 &lt; 350</strong> (consider if &gt; 350 in some situations)</td>
<td>2NRTI (ABC/3TC or TDF/FTC) + NNRTI (NVP or EFV) or bPI (FPV/r or LPV/r or SQV/r)</td>
<td>Guided by resistance testing</td>
<td>VL &gt; 500-1000</td>
</tr>
<tr>
<td><strong>BHIVA (2008)</strong></td>
<td><strong>CD4 &lt; 350</strong> (consider if &gt; 350 in some situations)</td>
<td>2NRTI (TDF/FTC) + NNRTI (EFV)</td>
<td>Guided by resistance testing</td>
<td>VL &gt; 400</td>
</tr>
<tr>
<td><strong>WHO EURO (2007/2008)</strong></td>
<td><strong>CD4 between 200-350</strong></td>
<td>2NRTI (ABC/3TC or AZT/3TC or TDF/XTC) + NNRTI (EFV)</td>
<td>2 NRTI (ABC/ddI or TDF/XTC or AZT/3TC or TDF/ABC or AZT/ddl) + bPI (LPV/r)</td>
<td>VL &gt; 400 (early failure) VL &gt; 1000-10,000 or 25% reduction in CD4 (late failure)</td>
</tr>
<tr>
<td><strong>WHO Global (2006)</strong></td>
<td><strong>CD4 &lt; 200</strong> (consider between 200-350 but start before reach 200)</td>
<td>2NRTI (AZT/3TC or TDF/XTC) + NNRTI (NVP or EFV)</td>
<td>2 NRTI (ABC/ddI or TDF/XTC or AZT/3TC) + bPI (ATV/r or LPV/r )</td>
<td>Clinical + CD4 (if available VL &gt; 10,000)</td>
</tr>
</tbody>
</table>

Vitoria MAA, 2008
When to start ART....

- 69% increase in mortality with treatment deferred till CD4+ <350/cu mm
- 94% increase in mortality with treatment deferred till CD4+ <500/cu mm
CIPRA HT 001 – Randomized controlled trial of earlier (CD4+ <350) versus deferred ART in Haiti

• Start ART at CD4+ <350/cu mm, compared to AIDS or CD4+ <200/cu mm
• 816 patients
• First line regimen: AZT, 3TC, EFV
• 23 deaths in deferred group, 6 in early treatment group
• 36 vs 18 cases of TB in deferred vs early treatment group
• DSMB recommended immediate ending of trial

(Pape J, Fitzgerald D et al, 2009)
Implications of Earlier ART

Kenya

Cost savings
↓ hosp care
↓ OI & TB rates
↓ AIDS mortality
↓ IRIS
↓ new HIV in children & adults?

?? Improve or worsen retention
? HIV DR

Added costs
↑ need for CD4
↑ # on ART
↑ if safer, better tolerated regimens
First line regimens, 2003-2005
3 most common regimens by region

Source: Egger M, CROI 2007
Balancing risk: dilemmas for HIV-positive mothers

HIV transmission from breastfeeding

Infectious diseases, malnutrition, mortality from not breastfeeding

CROI 2008: #45aLB

Timothy Thomas*1, R Masaba2, R Ndivo2, C Zeh1, C Borkowf3, M Thigpen3, K De Cock4, P Amornkul4, A Greenberg3, M Fowler3, and Kisumu Breastfeeding Study Team
1CDC Kenya, Kisumu; 2Kenya Med Res Inst, Kisumu; 3CDC, Atlanta, GA, US; and 4CDC Kenya, Kisumu
Guidelines and practice....

Maternal deaths per 100,000 live births, 2005

Median CD4 counts at start of ART Trends over time

World Health Organization

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"The arc of the moral universe is long but it bends towards justice"

Martin Luther King, 1929 - 1968
Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HELLER

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its effects.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors.

have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.
Tuberculosis – standardized therapy, safe therapy, everywhere....
The health sector and universal access to HIV prevention, treatment, care and support

**Now**

- Treatment
- Prevention

**From now on**

- Rx for adults
- Rx for children
- Rx for prevention
  - Essential care
  - Positive prevention
  - Male circumcision
  - Other prevention
  - Harm reduction

- Treatment scale-up in adults and children
- Integrated prevention and treatment
- Expanded role for ART in HIV prevention
- Combination prevention
- Interventions stratified by serostatus

- Only 3 million on ART
- Prevention and treatment disjointed
- Continuing high HIV incidence
- Definition of UA unclear
"Only those who dare to fail greatly can ever achieve greatly."

Robert F. Kennedy, 1925 - 1968