Current Status and Future of HIV Surveillance

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HIV and Drug Resistance Surveillance and Testing
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Outline

• HIV surveillance
  – Review of current approaches
  – New directions
• HIV surveillance among TB patients
  – Current recommendations
  – As sentinel population
  – In era of expanded HIV treatment
• Ethical considerations
Surveillance

• The routine collection of data about disease frequency and distribution; the analysis of those data; and the dissemination of that information to those who need to know.

• Information to answer three questions:
  – How big is the problem?
  – Where and to whom should limited resources go?
  – Is the problem getting better with my interventions?
HIV Surveillance
HIV Prevalence in Adults, 2004

39.4 million people living with HIV as of end 2004

HIV/AIDS Surveillance Data Points

- "RISK" SURVEILLANCE
- HIV INCIDENCE SURVEILLANCE
- HIV PREVALENCE SURVEILLANCE
- AIDS CASE SURVEILLANCE
- AIDS DEATHS

"WINDOW" PERIOD
ASYMPTOMATIC PERIOD
HIV ILLNESS or AIDS
DEATH

- = VIRAL LOAD
- = HIV ANTIBODIES
### What Questions Can HIV Surveillance Answer?

<table>
<thead>
<tr>
<th>Question</th>
<th>Surveillance method</th>
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</table>
| How many HIV-infected persons?    | • HIV sentinel surveillance  
                                 | • Population-based surveys                               |
| Is HIV prevention working?        | • Behavioral surveys                                    |
|                                   | • HIV/STD sentinel surveillance                          |
|                                   | • Population-based surveys                               |
|                                   | • HIV incidence                                          |
| Is HIV treatment working?         | • AIDS case reporting                                    |
|                                   | • Sample vital registration                              |
|                                   | • Cohort analysis of persons in care                     |
|                                   | • ARV resistance surveillance                            |
Surveillance Approaches to Monitor HIV

- **HIV incidence**
  - HIV prevalence in young persons
  - Serologic techniques

- **HIV prevalence**
  - Sentinel surveys
  - Population-based surveys

- **AIDS incidence**
  - AIDS-case reporting

- **AIDS mortality**
  - Vital registration

- **Behaviors linked with HIV**
  - Behavioral surveillance
# Classification of HIV Epidemic States

<table>
<thead>
<tr>
<th>Category</th>
<th>HIV Prevalence</th>
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<tbody>
<tr>
<td>Generalized HIV epidemic state</td>
<td>HIV prevalence consistently &gt; 1% among pregnant women</td>
</tr>
<tr>
<td>Concentrated HIV epidemic state</td>
<td>HIV prevalence consistently &gt;5% in at least 1 defined sub-population (e.g. IDUs, SWs, MSM; HIV prevalence &lt;1% among pregnant women)</td>
</tr>
<tr>
<td>Low-level HIV epidemic state</td>
<td>HIV prevalence has not consistently exceeded 5% in any defined sub-population</td>
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</table>
Primary Method of HIV Surveillance

• Industrialized countries
  – AIDS case surveillance

• Low resource settings
  – Antenatal sentinel surveillance
    • Unlinked anonymous testing (UAT) and use of PMTCT data
  – Poor vital registration and little mortality data
Sentinel Surveillance
Sentinel Surveillance

• The system by which “specific sites and population groups are selected, a predetermined number of persons are routinely tested, and testing is performed in a regular and consistent way.” (WHO)
Sentinel Surveillance Populations in Developing Countries

- Pregnant women in antenatal clinics
- Blood donors
- Military recruits and personnel
- STD clinic attenders
- Commercial sex workers
- Tuberculosis patients
- Hospitalized patients
HIV Antenatal Sentinel Surveillance

- Monitoring HIV prevalence in the general population recommended for countries with generalized HIV epidemics
- Most common method used is HIV sentinel surveillance in antenatal clinics
- Blood that is left-over after routine testing (such as syphilis testing) is stripped of all identifiers and tested for HIV anonymously (e.g. unlinked, anonymous testing (UAT) which is unconsented)
HIV Antenatal Sentinel Surveillance

- **Strengths**
  - Does not require extensive resources
  - Provides trend information
  - Already implemented for several years in many countries

- **Weaknesses**
  - May overestimate prevalence in younger women and under-estimate in older women
  - Tend to have been concentrated in urban areas
  - Excludes men
HIV/AIDS Surveillance in the First Decade of the Epidemic

- Mainly HIV sentinel surveillance and AIDS reporting
- Did not make best use of other data sources
- Provided poor early warning
- Ignored at-risk subpopulations
Second-Generation HIV Surveillance

- Developed by the WHO and UNAIDS as a response to the increasing complexity of the HIV epidemic
- Outlines more sophisticated surveillance activities
- Provides a more comprehensive understanding of epidemic trends
- Improves effectiveness of control and prevention efforts
Components of Second-Generation HIV Surveillance

• Behavioral surveillance

• HIV/AIDS case reporting

• Death registration

• Sexually transmitted infection (STI) surveillance
Goals of Second-Generation HIV Surveillance

• Better understanding of trends over time
• Better understanding of behaviours driving the epidemic in a country
• Increased focus on sub-populations at highest risk for infection
• Triangulation of data sources
• Flexible to change with the stage of epidemic
### 2nd Generation HIV Surveillance: Providing Key Answers

<table>
<thead>
<tr>
<th>HIV epidemic</th>
<th>Questions for surveillance</th>
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<tbody>
<tr>
<td>Low-level and</td>
<td>• Any risk behaviour leading to HIV epidemic?</td>
</tr>
<tr>
<td>Concentrated</td>
<td>• Sub-populations with risk behaviour?</td>
</tr>
<tr>
<td></td>
<td>• Sub-populations: size? HIV prevalence? Behaviours?</td>
</tr>
<tr>
<td></td>
<td>• Links between these sub-populations and general pop.?</td>
</tr>
<tr>
<td>Generalized</td>
<td>• What are the trends in HIV infection?</td>
</tr>
<tr>
<td></td>
<td>• Do trends in behaviour explain trends in HIV prevalence?</td>
</tr>
<tr>
<td></td>
<td>• Impact of interventions on risk behaviours?</td>
</tr>
<tr>
<td></td>
<td>• Impact of HIV epidemic on individual, family and country?</td>
</tr>
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</table>
Population-Based Surveys
General Population-Based Surveys

- HIV seroprevalance survey using a nationally representative sample of households
- Increasingly popular; often linked to Demographic and Health Surveys (DHS)
- Uses consented anonymous method for HIV testing
General Population-Based Surveys

- **Strengths:**
  - Includes rural areas
  - Can be linked to behaviors and other additional variables
  - Includes men

- **Weaknesses:**
  - Costly
  - Non-response bias, especially men
  - Not optimal to follow trends
# Estimated National HIV Prevalence from ANC Sentinel Surveillance and DHS

<table>
<thead>
<tr>
<th></th>
<th>Sentinel Surv</th>
<th>DHS</th>
<th>Difference (%)</th>
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<tbody>
<tr>
<td>Zambia</td>
<td>21.5%</td>
<td>15.6%</td>
<td>-27.4%</td>
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<tr>
<td>Mali</td>
<td>2.1%</td>
<td>1.7%</td>
<td>-19%</td>
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<tr>
<td>Kenya</td>
<td>9.4%</td>
<td>6.7%</td>
<td>-28.7%</td>
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</table>
Modeling and Estimates
Modeling and Estimates

• Modeling is used to provide estimates of:
  – # of persons living with HIV
  – # of orphans
  – # of persons with advanced HIV disease
  – # of persons dying from HIV

• Data dependent upon ANC sentinel surveillance, or HIV sentinel surveillance in high risk groups
Ethiopia: The HIV/AIDS Pyramid, 2001

Reported: 15,202 AIDS Cases

Estimated: 219,400 AIDS cases

Estimated: 2.2 Million PLWHA

Number of Orphans 1.2 Million
Morbidity and Mortality Surveillance
AIDS Surveillance

• Recommended for all countries but only really used in industrialized countries

• Reporting from resource-constrained countries estimated to be 10 - 20%

• There are 8 AIDS case definitions currently in existence many of which do not coincide with WHO clinical staging
AIDS Surveillance

• **Strengths**
  – Ability to monitor impact of treatment when have complete consistent reporting

• **Weaknesses**
  – Many case definitions
  – Forms or mechanism to report often not present
  – Often unable to diagnose conditions due to lack of laboratories, x-rays or other diagnostic equipment
Longitudinal Surveillance of Treatment under the Emergency Plan (LSTEP)

Objectives

• Describe process & outcomes in adults and children
  – Time from eligibility to entry into ART program
  – Retention in ART program and time to event (change, stop, transfer, death)
  – Adherence to ART regimen
  – Regimen use, change, and reason for change
  – Change in health status (e.g. active TB, hospitalization, CD4)
  – Receipt of basic HIV care services

• Analyze process and outcomes by individual, program, and facility variations
Mortality Surveillance

- Great advocacy tool for industrialized countries

- Vital registration systems are very poor in most resource-constrained settings

- In-depth sites (community worker collects information on all births and deaths) exists through Africa and Asia

- Exploring feasibility of using special vital registration with verbal autopsy in focus countries
New Directions

• HIV incidence surveillance

• Antiretroviral drug resistance

• Use of programmatic data
Test Considerations

- A two test strategy (Strategy II) is recommended irrespective of HIV prevalence
- Testing in-country is best performed decentralized to allow for capacity building in regional or zonal laboratories
- Rapid tests, automated EIA and combinations are appropriate for the two test strategy
- The Western blot assay is not recommended for surveillance testing
- An acceptable level of discordance during serial testing should be calculated based on HIV prevalence and particular test algorithm in use
Early HIV Infection

Seroconversion to Ab cutoff

Antibody cutoff
Quantity
Proportion
Avidity
Isotype
Specificity

Days

Response

infection

RNA+ Ab-
P24+ Ab -

RNA
p24
Ab
The HIV-1 BED Incidence EIA

- Competitive capture format of the assay (HIV-IgG and non-HIV-IgG)
- Indirectly measures increasing levels of HIV-IgG as a proportion of total IgG
- The assay is not subtype dependent
- The assay is not affected by variation in dilution
- The assay has been evaluated for inter-run, intra-run, and inter-operator variability
WHO/HIVResNet HIVDR Surveillance: A Strategy to Evaluate Transmitted HIVDR

- Some degree of HIV drug resistance (HIVDR) is inevitable because:
  - Lifelong treatment, no cure
  - High rate of mutation
- Small unrepresentative studies are often the only source of information available
- Overestimates of transmitted HIVDR could lead to harmful policy decisions and misuse of drugs and fuel arguments of those not wanting ART scaled up
- To produce reliable information about prevalence and trends of HIV DR transmission, there is the need for a dedicated standardized HIVDR surveillance system
WHO/HIVResNet HIVDR Surveillance (2)

• “Minimizing HIVDR” = reducing the rate of emergence and spread of HIVDR and limiting its public health consequences

• WHO proposes use of HIVDR Threshold Surveys
  – Focus on geographic areas and sites where transmission of resistance is most likely to be seen first
  – Use specimens and information already being collected, if possible
  – Categorize prevalence of transmitted resistance in 3 level: <5%, 5-15%; >15%
WHO/HIVResNet HIVDR Surveillance (3)

- Region/country specific progress:
  - Africa: Tanzania, Kenya, Mozambique, Malawi, Botswana, South Africa, Ethiopia
  - SE Asia: India, Thailand, Indonesia
  - Western Pacific: China, Vietnam
  - Europe: Ukraine, Russia
  - Eastern Mediterranean: Iran, Morocco
  - Americas: Brazil, Honduras

- Using standard protocol in context of routine HIV surveillance, no additional questionnaire, no additional blood draw

- For this to be possible, the specimen quality has to be handled differently for routine and DRS. Assessment visit required
WHO/HIVResNet HIVDR Surveillance (4)

Challenges
- Global WHO/HIVResNet (advisory and implementing body) leadership, coordination
- Working with major partners GFATM, USG, EC, WB, donors
- Standardized approach
- Capacity at country level
- Link to HIV Surveillance and ART Care
- Fund Raising globally and locally
- HIV/resLab network, beginning to be set up. QA process is an additional challenge for SRLs, will use proficiency panels
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HIV Surveillance among TB Patients
Estimated TB incidence vs HIV prevalence

Source: WHO
WHO Recommendations for TB/HIV Surveillance
New Policy on HIV Testing

“Diagnostic HIV testing is indicated whenever a person shows signs or symptoms that are consistent with an HIV-related disease or AIDS...This includes HIV testing for all tuberculosis patients as part of their routine management.”

UNAIDS/WHO Policy Statement on HIV Testing

June, 2004
New Guidelines for HIV Surveillance in TB Patients

1. Periodic (special) surveys
2. Sentinel methods
3. Data from routine HIV testing of TB patients

### Guidelines for HIV Surveillance in TB Patients

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Recommended HIV Surveillance Methods</th>
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<tbody>
<tr>
<td>Generalized HIV epidemic state</td>
<td>Data from routine HIV testing of TB patients and periodic (special) or sentinel surveys</td>
</tr>
<tr>
<td>Concentrated HIV epidemic state</td>
<td>Data from routine HIV testing of TB patients or periodic (special) or sentinel surveys</td>
</tr>
<tr>
<td>Low-level HIV epidemic state</td>
<td>Periodic (special) or sentinel surveys</td>
</tr>
</tbody>
</table>

Rationale for HIV Surveillance in TB Patients (1)

• TB patients as sentinel population
  – For HIV surveillance
  – For HIV morbidity/mortality surveillance
  – To estimate number of ARV candidates
HIV prevalence of TB Patients in Cambodia

Thailand
- Oudor Meanchey: 12.9% (4/31)
- Banteay Meanchey: 11.6% (10/86)
- Siem Riep: 12.5% (27/216)
- Pursat: 5.6% (4/72)
- Battam Bang: 13.2% (14/106)
- Pailin: 33.3% (2/6)

Laos
- Preah Vinear: 3.7% (1/27)
- Stung Treng: 6.7% (1/15)
- Rattana Kiri: 10.0% (1/10)
- Kratie: 10.9% (5/46)

Viet Nam
- Kompong Cham: 5.4% (11/205)
- Kompong Thom: 1.7% (2/115)
- Kompong Chhnang: 5.5% (6/109)
- Phnom Penh: 5.4% (11/205)
- Prey Veng: 10.4% (22/211)
- Kandal: 6.8% (15/221)
- Takeo: 6.6% (9/137)
- Kampot: 6.6% (9/137)
- Krong Kep: 25.0% (1/4)
- Kompong Som: 33.3% (11/33)

Total HIV prevalence: 11.8% (265/2244)

Percent HIV Seroprevalence in TB Patients, Selected African Countries, 1988-1997 (WHO)

- Abidjan, CIV
- Kampala, UGA
- Hlabisa, SAFR
- Lusaka, ZAM
- Blantyre, MAL

% HIV Seropositive TB Cases

0 10 20 30 40 50 60 70 80
Rationale for HIV Surveillance in TB Patients (2)

- Expand HIV testing of TB patients
- Foster information sharing between NTP, NACP, surveillance programs
- Understand TB/HIV epidemiology
- Target resources and planning
- Evaluate impact of interventions
Expand HIV Testing of TB Patients

• Prerequisite for
  – Surveillance using routine clinical data
  – HIV care and treatment for TB patients
• Identifies antiretroviral (ARV) candidates
• Contributes to HIV prevention
Foster Information Sharing

- HIV testing infrastructure
- Modification of forms and registers
- Potential linkage of existing surveillance systems
- Implementation/enhancement of referral networks
Understand TB/HIV Epidemiology

- Assess trends
- Stratified cohort analysis
  - Case fatality and default rates
- Monitor impact of changing HIV seroprevalence on TB incidence
- Understand association between HIV and TB drug resistance
Seroprevalence of HIV in New TB
Thailand, 1990-2002

- Region 10 (North)
- National
Evaluate Impact of Interventions

- Acceptance of HIV testing
- Utilization of services
- Trends in TB incidence
- Stratified cohort analysis
  - Effects on case fatality rates
- Uptake and impact of ARVs, cotrimoxazole
- Track patient disposition after TB treatment
TB-AIDS Cases as a Percentage of All TB Cases by Region, US, 1993-2002*

*Preliminary data
Challenges for HIV Surveillance in TB Patients

- Expansion of HIV testing
- Use of routine clinical data
- Modifying and linking TB and HIV surveillance systems
- Ethical considerations
  - Confidentiality
  - Continuity of care
  - Provision of test results
Ethical Considerations
Definitions

• Anonymous
  – No identifiers ever collected
• Anonymized
  – Identifiers removed
• Confidential
  – Identifying information kept confidential
• Informed consent
  – Risks/benefits of participation clearly explained
Confidentiality

• All patient medical information confidential
  – HIV > TB
• Optimal clinical care requires knowing sensitive information
• Share on “need to know” basis
  – Persons providing direct clinical care
• Documents should be stored in secure location
  – TB registers, ART registers
• Destroy unnecessary/duplicate paperwork
<table>
<thead>
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TB Patients

• Blood not routinely collected
• ? If UAT (without consent) is ethical
• Other linked/unliked methods can be used
• HIV testing of sputum specimens
  – Remnant specimens can be used
  – Lower sensitivity and specificity
  – Not recommended where expected HIV prevalence < 10%
Unlinked Anonymous Testing (UAT): CDC Recommendations

• Ethical if:
  – Performed on remnant ("left over") specimen
  – Community is aware of survey
  – True anonymity
  – Local access to counseling and testing available
  – Data used to benefit community
Conclusions

HIV surveillance
- More and better-quality data:
  - More surveillance sites with better representation of rural population
  - More planning and better oversight
  - More accurate estimates and projections
- New methods:
  - Population surveys with biomarkers
  - Serologic methods for incidence estimation
- Answering new questions:
  - Impact of prevention and care interventions

HIV surveillance in TB patients
- Rationale for performing has changed
- Need to look for synergies with HIV surveillance activities
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