Unit 5, part 1: The DOTS strategy for controlling TB

Objectives

By the end of this subunit, participants will be able:
1) to describe the DOTS strategy (the WHO-recommended strategy for controlling TB); and
2) to discuss the implications of the strategy for implementing collaborative TB/HIV activities.

Methods

Plenary presentation: The DOTS strategy
Plenary discussion

Materials

Document 5.1: The DOTS strategy (slides)
Document 5.1

The DOTS strategy for controlling TB

Document No. 5.1

TB/HIV course for managers at the national and subnational levels

Objectives of the sub-unit

- To describe the DOTS strategy (the WHO-recommended strategy for controlling TB)
- To discuss the implications of the strategy for implementing collaborative TB/HIV activities

History of DOTS

1980s: Styblo defines International Union against Tuberculosis and Lung Diseases model to control TB in the United Republic of Tanzania
1991: World Health Assembly establishes the 70/85 targets for 2000
1993: WHO declares TB as a global emergency
1994: New TB control framework
1995: DOTS launched as a WHO strategy
1998: London Committee, StopTB Partnership launched
2000: Amsterdam Declaration; targets in 2005
2001: Six working groups and Global Drug Facility launched
2001: Global Fund to Fight AIDS, Tuberculosis and Malaria, Millennium Development Goals and Washington Commitment
2002: Expanded framework DOTS brand name

The DOTS strategy

is a comprehensive strategy that ensures cure to most people with TB disease presenting to primary health care services.


DOTS

- Government commitment to ensuring sustained, comprehensive TB control activities
- Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services
- Standardized short-course chemotherapy using regimens of 6–8 months for at least all confirmed smear-positive cases. Good case management includes directly observed therapy during the intensive phase for all new sputum-positive cases, the continuation phase of rifampicin-containing regimens and the whole re-treatment regimen.
- A regular, uninterrupted supply of all essential anti-TB drugs
- A standardized recording and reporting system that allows assessment of case-finding and treatment results for each patient and of the TB control programme performance overall

Aspects of DOTS

- Technical
- Logistical
- Operational
- Political

Aspects of DOTS

Technical
- Case detection and diagnosis
- Standardized short-course chemotherapy
- Direct observation during the initial phase of treatment (DOT)
- Recording and reporting of progress and cure

Justification for Directly Observed Treatment (DOT)

About one third of patients do not take medications regularly as prescribed

Perhaps one third of patients who do take medications make errors in self-administration.


Aspects of DOTS

Logistical
- Dependable drug and diagnostic supply
- Laboratories for microscopy
- Supervision and training of health workers

Aspects of DOTS

Operational
- Five basic core elements
- Flexibility in implementation

Three phases to gradual DOTS implementation
1. A pilot project phase
2. An expansion phase
3. A maintenance phase

Aspects of DOTS

Political
- Government commitment
- Policy formulation
- Resource mobilization
A strategy for quality

<table>
<thead>
<tr>
<th>Detection</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive, risk group</td>
<td>Passive, risk group</td>
<td>Active, population screening</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostics</th>
<th>Three smear + limited X-ray</th>
<th>Extensive X-ray or fluoroscopy</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear-positive, smear-negative, extrapulmonary, new, relapse, treatment after interruption, failure, transfer in</td>
<td>Weak</td>
<td>Extensive X-ray or fluoroscopy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized, DOT</td>
<td>Individual, inadequate, decentralized, cheap</td>
<td>Weak</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2, 4, 6 or 2, 5, 8 smear</td>
<td>2, 4, 6 or 2, 5, 8 smear</td>
<td>No systematic, X-ray</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recording and reporting</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard system</td>
<td>No records, not done</td>
<td>No records, not done</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cure</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliable cohort</td>
<td>Reliable cohort</td>
<td>Unreliable outcome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result</th>
<th>DOTS</th>
<th>Non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success, cost-effective</td>
<td>Not evaluated</td>
<td>Multi-drug resistance, expensive</td>
</tr>
</tbody>
</table>

DOTS is more than

- DOT
- Only five components (but: planning, budgeting, financing, training, supervision, mapping, staff management, data analysis and assessment)
- Strictly five components (but: flexible DOT in low incidence, culture and drug susceptibility testing, X-ray and DOTS Plus)

Treatment outcomes by WHO region:

<table>
<thead>
<tr>
<th>Treatment outcomes by WHO region: DOTS versus non-DOTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001 cohort</td>
</tr>
</tbody>
</table>

Dynamics of pulmonary TB in Peru

Pulmonary TB cases per 100,000

- DOTS 1990
- Case-finding
- Pulmonary TB declining 6% per year

Progress towards the 70/85 targets

<table>
<thead>
<tr>
<th>Progress towards the 70/85 targets</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Treatment success (%)</th>
<th>DOTS detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 20 40 60 80 100</td>
<td>0 20 40 60 80 100</td>
</tr>
</tbody>
</table>

WHO-recommended global strategy to stop TB and reach the Millennium Development Goals for 2015

- Pursuing expansion and enhancement of high-quality DOTS
  - Political commitment
  - Case detection through bacteriology
  - Standardized treatment, with supervision and patient support
  - Effective drug supply system
  - Monitoring system and evaluation of impact

- Additional components
  1. Addressing TB/HIV and multi-drug-resistant TB
  2. Contributing to strengthening health systems
  3. Engaging all care providers
  4. Empowering patients and communities
  5. Enabling and promoting research
The anchor of the WHO-recommended global strategy: pursue expansion and enhancement of high-quality DOTS

- Political commitment with long-term planning, adequate human resources and expanded and sustainable financing to reach the targets set by the World Health Assembly and the Millennium Development Goals
- Case detection through bacteriology (microscopy first and then culture and drug susceptibility testing) and strengthening the laboratory network to facilitate detection of TB cases that are sputum smear-positive and -negative, drug-resistant and multi-drug-resistant
- Standardized treatment, under proper case management conditions, including DOT to reduce the risk of acquiring drug resistance, and patient support to increase adherence and the chance of cure
- An effective and regular drug supply system, including improving drug management capacity
- An efficient monitoring system for supervising and evaluating programmes, including measuring impact

The other five components of the WHO-recommended global strategy

2. Addressing TB/HIV, multi-drug-resistant TB and other special challenges by scaling up TB/HIV joint activities, DOTS Plus and other relevant approaches

3. Contributing to strengthening health systems by collaborating with other health programmes and general services in, for example, mobilizing the necessary human and financial resources for implementation and evaluating impact and by sharing and applying the achievements of TB control

4. Engaging all care providers, public, nongovernmental and private, by scaling up public-private mix approaches to ensure adherence to the international standards of TB care, with a focus on the providers for the poorest people

5. Empowering patients and communities by scaling up community TB care and creating demand through context-specific advocacy, communication and social mobilization

6. Enabling and promoting research to improve programme performance and for developing new drugs, diagnostics and vaccines

Quality TB care for all: ensure a high standard

- Patient care to cure and prevent TB is the ultimate goal of DOTS.
- The foundation of DOTS is effective patient care that alleviates suffering and controls and prevents TB in a community.
- A standard of care for TB exists already, and is evidence-based, but needs to be further promoted among all care providers.
- Simply, each care provider, public or private, should:
  - Diagnose TB quickly (bacteriological confirmation)
  - Treat TB properly (short-course chemotherapy and treatment support)
  - Report TB cases and treatment outcomes
- If all providers did the right thing, TB would be controlled.
Unit 5, part 2: Clinical management of TB

Objectives

By the end of this subunit, participants will be able:
1) to describe how the clinical management of TB is organized;
2) to state the principles of diagnosis, treatment and case management related to controlling TB; and
3) to discuss the implications of these principles for implementing collaborative TB/HIV activities.

Methods

Plenary presentation: Clinical management of TB
Exercise
Plenary discussion

Materials

Document 5.2: Clinical management of TB (slides)
Document 5.3: Introduction to the exercise for Unit 5
Document 5.2

Clinical management of TB
Document No. 5.2

TB/HIV course for managers at the national and subnational levels

Objectives of the subunit

• To describe how the clinical management of TB is organized
• To state the principles of diagnosis, treatment and case management of TB
• To discuss the implications for collaborative TB/HIV activities

Organization of clinical management: objective

• To ensure that the drug regimen is regularly taken until cure

Organization of clinical management: factors

• Patient’s access
  – distance, time, cost, acceptability
• Regular drug supply
• Duration and periodicity of treatment
  – daily, intermittent
• Direct observation of treatment (DOT)
• Drug presentation
  – blister pack, fixed-dose combination, patient kit

Diagnosis versus case detection

• Diagnosis: health care activity performed on people consulting for symptoms or signs
• Main objective: curing the patient
• Uses all methods available, and covers all ages, sites and forms of the disease
• Is followed by information to the patient and prescription of treatment
• Treatment is patient’s responsibility

Diagnosis versus case detection

• Case detection: control programme activity, mainly to find sources of infection: smear-positive pulmonary cases
• Mainly by sputum smear examination in people with cough of long duration
• To shorten infectivity, reduce the risk of infection to the community, mortality and morbidity (contacts and high-risk groups)
• Must be followed by information to the person with TB and treatment (programme responsibility)
Case detection

• Active and passive are obsolete terms
• All diagnosis is passive (patient demand)
• All case detection is active
  – contacts
  – High-risk groups
  – suspects with cough in health facilities
• The key is correct selection of the target population and the method

Case detection

**Sputum smear examination**

• Rapid results
• Correlates with infectivity
• Detects the main sources
• Without HIV, correlates with severity
• Technique allows decentralization
• Less costly than culture

Case detection

**Sputum smear examination**

• Three smears detect >60% of pulmonary TB
  >95% of the most infectious cases
• One smear detects ~75% of smear-positive, the second adds ~20% and the third ~5%
• Spot/overnight/spot maximizes results
• Reduces the number of visits (patient cost)
  – spot is immediately available
  – overnight is the best quality
• Error (disagreement) <5%

Case detection

**Sputum culture**

• Allows confirmation of *M. tuberculosis*
• Detects lower concentration (100 bacteria/ml)
• One culture detects ~80% of culture (+)
• Does not identify most infectious cases
• Long delay until results available
• More complex than smears (central laboratory)

Case detection

**Radiology**

• As a diagnostic tool
  – useful for differential diagnosis and site
  – rapid
  – requires expert interpretation
  – under-reading 20–30%, over-reading 1–20%
  – does not confirm diagnosis
  – less useful for TB among people living with HIV/AIDS
• As a monitoring tool
  – inter- and intrareader disagreement >20%
  – shadows (scars) do not mean active disease

Case detection

**Radiology**

• As a case detection method
  – does not identify most infectious sources
  – ~12% of positive cases missed, ~37% unconfirmed
• In mass examination (MMR)
  – most cases detected through symptoms
  – does not detect incidence (75% of cases in Kolin District)
  – smear and culture (+) develop in <1 year
  – costly
  – leads to over-diagnosis
  – patients not motivated for treatment
**Case detection**

Smear (+) infect ~10 times more than (–)

Where to find sources (actively)?
- In the community
  - Prevalence is low (1–2 per 1000)
  - Does not detect the true incidence
  - Is costly and complex
  - Patients detected are not motivated for treatment
- In high-risk groups
  - Rationale if abnormal X-ray, contacts, prisons
  - If high prevalence (1–10%)
  - They are usually a small number

**Case detection**

- The best indicator of case detection is the number of people with cough examined for diagnosis (district level).
- The positivity of smears and bacillary load are operational (during expansion) and then epidemiological indicators.
- In health facilities, the percentage of outpatients examined is an indicator of detection.
- The denominator can be easily studied.

**Case detection: conclusions**

- Smear examination: rapid detection of sources to reduce risk of infection (treatment monitoring)
- Culture: confirms TB disease (+ treatment monitoring)
- Radiology: helps clinical diagnosis (+ screening high-risk group)

Diagnosis of adult pulmonary TB should include smear results (positive or negative)

**Case detection**

Screening for cough in outpatient department
- Cough is a common outpatient symptom
- Screening is rapid and inexpensive
- 3–10% of general adult outpatients may have cough of over two weeks’ duration
- 1–10% are smear-positive for TB
- Many attend for other reasons (including child vaccination)
- People with TB disease visit health facilities several times before diagnosis

**Case detection: definitions**

- TB suspected: with symptoms or signs of TB
- Case of TB: a person bacteriologically confirmed or diagnosed by a clinician
- Definite case of TB: culture-positive or with two positive sputum smears

**Standardized TB treatment regimens**

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>People with TB disease</th>
<th>Initial phase</th>
<th>Continuation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Daily or 3 times weekly</td>
<td>Daily or 3 times weekly</td>
</tr>
<tr>
<td>1</td>
<td>New sputum smear positive (new smear or smear negative previously)</td>
<td>Isoniazid + Rifampicin + Pyrazinamide + Ethambutol for 2 months (2 HRZE)</td>
<td>Isoniazid + Rifampicin for 4 months (4 HR) or Isoniazid + Ethambutol daily for 6 months (6 HE)</td>
</tr>
<tr>
<td>2</td>
<td>Previously treated sputum smear positive, rapid resistance after failure</td>
<td>Isoniazid + Rifampicin + Pyrazinamide + Ethambutol + Streptomycin for 2 months (2 HRZES) followed by Isoniazid + Rifampicin + Pyrazinamide + Ethambutol for 1 month (1 HRZE)</td>
<td>Isoniazid + Rifampicin for 4 months (4 HR) or Isoniazid + Ethambutol daily for 6 months (6 HE)</td>
</tr>
<tr>
<td>3</td>
<td>New sputum smear negative (other than category 1)</td>
<td>Isoniazid + Rifampicin + Pyrazinamide + Ethambutol for 2 months (2 HRZE)</td>
<td>Isoniazid + Rifampicin for 4 months (4 HR) or Isoniazid + Ethambutol daily for 6 months (6 HE)</td>
</tr>
<tr>
<td>4</td>
<td>Chronic or multidrug-resistant TB (new sputum smear positive after supervised re-medication)</td>
<td>Specially designed standard or individualized regimen</td>
<td></td>
</tr>
</tbody>
</table>
Organization of treatment (1)

Initial phase alternatives
- Hospitalization (daily treatment)
- Costly, helps patient but not family
- Food, rest, specialists not critical
- Allows direct observation of intake
- Ambulatory (daily or three times weekly)
- Accessible, acceptable, allows work
- Requires well-organized supplies, staff
- Requires organization of DOT

Organization of treatment (2)

Initial phase alternatives
- 3 or 4 drugs
  - severity, load of bacilli, HIV, resistance
- Fixed-dose combinations
  - ensures all-or-none intake
  - practical to define dosage by weight
- Patient kits
  - ensures full supply
  - facilitates ordering and distribution

Organization of treatment (3)

Continuation phase alternatives
- Isoniazid + rifampicin 6 months (observed) or isoniazid + ethambutol 8 months
  - Isoniazid + rifampicin more effective, mainly in HIV-positive people
- “Daily” or three times per week
  - Three times is better for observed treatment, less costly for patient, allows time for retrieval
- Fixed-dose combinations, blister packs and patient kits

Treatment delivery process
- Integrated activity including:
  - Appropriate regimen (quality proven, properly selected, right dose, given at the right time …)
  - This involves the drug management cycle, the training and capacity-building component of the programme and the health education (to the patient) component
  - The DOT component
Document 5.3

Introduction to the exercise for Unit 5

For this exercise, your facilitator will divide the participants into groups of three. The purpose of the exercise is to analyse the implementation of the DOTS strategy in “Fictitia”, identify gaps and propose activities to address the gaps.

• Read pages 140-148 in the report from Fictitia in Annex 1

• Analyse what the national TB control programme has done so far for implementing the DOTS strategy in the country in relation to WHO recommendations for a public health approach, with special focus on:
  1) organization of the TB diagnosis and treatment services;
  2) standardization of TB treatment regimens;
  3) provision of isoniazid preventive therapy; and
  4) collaboration between the TB and HIV/AIDS programmes.

• Identify immediate gaps in the programme (especially in terms of strengthening the capacity of the health system) and propose priorities for your planning.

• Prepare to present the group work in the plenary session.

Tell a facilitator when you are ready for the plenary discussion.
Unit 6, part 1: Universal access to antiretroviral therapy

Objectives

By the end of this subunit, participants will be able:
1) to describe universal access to antiretroviral therapy (rationale, core premises and principles, targets, objectives, and components of its strategic framework); and
2) to discuss the implications of universal access to antiretroviral therapy for implementing collaborative TB/HIV activities.

Methods

Plenary presentation: Universal access to antiretroviral therapy
Plenary discussion

Materials

Document 6.1: Universal access to antiretroviral therapy (slides)
Document 6.2: UNAIDS/WHO policy statement on HIV testing (1)
Universal access to antiretroviral therapy

Document No. 6.1

TB/HIV course for managers at the national and subnational levels

Objectives of the subunit

• To describe universal access to antiretroviral therapy (rationale, core premises and principles, targets, objectives, and components of its strategic framework)

• To discuss the implications of universal access for implementing collaborative TB/HIV activities

Myths about antiretroviral therapy

• Developing countries are too poor to afford antiretroviral drugs.

• Antiretroviral drugs are too complicated.

• Infrastructure to support antiretroviral therapy is insufficient:
  > Poor drug procurement and distribution systems
  > No laboratories to monitor resistance

• Inadequate human resources
  > To prescribe and monitor antiretroviral therapy use

• Everything must be in place before any action.

Why now?

• Six million people need antiretroviral therapy

• Only 1 million were receiving it by mid-2005

• Antiretroviral therapy offers hope
  > Has decreased death rates by up to 80% in Europe and the Americas
  > Drug prices continue to fall

• Unprecedented global political commitment

• New sources of financing – US$ 20 billion on the table:
  - Multilateral sources: World Bank, Global Fund to Fight AIDS, Tuberculosis and Malaria
  - Bilateral funding: United States President's Emergency Plan for AIDS Relief, United Kingdom Department for International Development, GTZ and Sweden

Antiretroviral therapy coverage in low- and middle-income countries, June 2005

<table>
<thead>
<tr>
<th>Geographical region</th>
<th>Number of people receiving antiretroviral therapy (low estimate – high estimate)</th>
<th>Estimated need</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>500 000 (425 000–575 000)</td>
<td>4 700 000</td>
<td>11%</td>
</tr>
<tr>
<td>Latin America and the Caribbean</td>
<td>290 000 (270 000–310 000)</td>
<td>465 000</td>
<td>62%</td>
</tr>
<tr>
<td>East, South and South-East Asia</td>
<td>155 000 (125 000–185 000)</td>
<td>1 100 000</td>
<td>14%</td>
</tr>
<tr>
<td>Europe and central Asia</td>
<td>20 000 (18 000–22 000)</td>
<td>160 000</td>
<td>13%</td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>4 000 (2 000–6 000)</td>
<td>75 000</td>
<td>5%</td>
</tr>
<tr>
<td>Total</td>
<td>970 000 (840 000–1 100 000)</td>
<td>6.5 millions</td>
<td>15%</td>
</tr>
</tbody>
</table>
Number of people receiving antiretroviral (ARV) therapy in low- and middle income countries, end 2002 to mid-2005

High burden countries in need of antiretroviral treatment, situation as of November 2003

Estimated number of people receiving ARV therapy and percentage coverage in 20 countries with the highest unmet need, June 2005

*Need people is expressed as the total number of people who need ARV therapy divided by 100 to indicate the number of people who need to be treated by the end of 2005.
Deaths per 100 person-years

Deaths per 100 person-years

Deaths

Deaths per 100 person-years

Percentage of patient-days on antiretroviral therapy

Mortality and use of antiretroviral therapy, 1995–2001

Deaths

Deaths per 100 person-years

Use of antiretroviral therapy

AIDS deaths in Africa

AIDS deaths in western Europe

Introduction of highly active antiretroviral therapy

Guiding principles

• Respect of ethical standards
• Universal and equitable access
• Paying attention to vulnerable groups
• Involving people living with HIV/AIDS
• Country in the driving seat
• Intensive partnership (countries, multilateral partners, bilateral partners, communities and the private sector)
• Innovation, learning and sharing

Strategic framework

1. Global leadership, strong partnership, advocacy
2. Urgent, sustained country support
3. Simplified standardized tools to deliver antiretroviral therapy
4. Effective, reliable supply of medicines and diagnostics
5. Rapid identification and reapplication of new knowledge and successes

Accelerating prevention

• Treatment and prevention must be scaled up together or the epidemic will continue
• Availability of treatment can reduce stigma and facilitate prevention
• Routine testing increases the numbers of people who know their HIV status
• Treatment has the power to mobilize funds to scale up prevention
Influence of TB lessons

- Target-driven
- Public health approach
- Integrate prevention with treatment
- Brand name
- Partnerships
- Standardization and harmonization
- Link people with TB disease to drug flow
- and many more ………

Treatment scale-up: countries that requested assistance as of March 2004

Technical assistance needs identified

<table>
<thead>
<tr>
<th>Field of technical assistance</th>
<th>% of countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capacity-building (tools and training)</td>
<td>60%</td>
</tr>
<tr>
<td>Medicines and diagnostics</td>
<td>56%</td>
</tr>
<tr>
<td>procurement, supply chain management, etc.</td>
<td></td>
</tr>
<tr>
<td>Monitoring and evaluation (patient-tracking system)</td>
<td>48%</td>
</tr>
<tr>
<td>Antiretroviral therapy (policy and equity issues)</td>
<td>44%</td>
</tr>
<tr>
<td>Human resources planning</td>
<td>32%</td>
</tr>
<tr>
<td>Testing and counselling</td>
<td>28%</td>
</tr>
<tr>
<td>Laboratory</td>
<td>20%</td>
</tr>
<tr>
<td>Antiretroviral therapy (policy and equity issues)</td>
<td></td>
</tr>
<tr>
<td>Program communication and advocacy</td>
<td>16%</td>
</tr>
<tr>
<td>Coordination and management (underestimated)</td>
<td>15%</td>
</tr>
<tr>
<td>Fundraising</td>
<td>8%</td>
</tr>
<tr>
<td>Community involvement</td>
<td>5%</td>
</tr>
<tr>
<td>Partnership</td>
<td>8%</td>
</tr>
</tbody>
</table>

Conclusions

- The most challenging public health intervention

- Considerable additional opportunities for developing health systems

- Monitoring and evaluation systems need to be reinforced and tailored to country needs
Unit 6, part 2: Clinical management of HIV/AIDS

Objectives

By the end of this subunit, participants will be able:

1) to describe how the clinical management of HIV/AIDS is organized;
2) to review the clinical and laboratory eligibility criteria for antiretroviral therapy, antiretroviral drug regimens and side-effects; and
3) to discuss the implications of these principles for implementing collaborative TB/HIV activities.

Methods

Plenary presentation: Clinical management of HIV/AIDS
Exercise
Plenary discussion

Materials

Document 6.3: Clinical management of HIV/AIDS (slides)
Document 6.4: Exercise
Document 6.5: Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach – 2003 revision (2)
Document 6.6: TB/HIV: a clinical manual (3)
Document 6.7: IMAI interim guidelines for first-level facility health workers (4)
Document 6.8: Participant manual for the WHO basic ART clinical training course (5)
Clinical management of HIV/AIDS

Document No. 6.3

TB/HIV course for managers at the national and subnational levels

Objectives of the subunit

- Describe the organization of clinical management of HIV/AIDS based on the WHO publication *Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach*

- Review the clinical and laboratory eligibility criteria for antiretroviral therapy and the side effects

- Discuss the implications for collaborative TB/HIV activities

Principles of the revised guidelines

- Review and update of 2002 guidelines

- Simplified and standardized antiretroviral therapy guidelines for WHO’s “3 by 5” strategy to allow rapid scale-up of treatment

- Targets resource-limited settings

- For use by national AIDS control programmes and other policy-makers

Scaling up antiretroviral therapy in resource-limited settings - Key elements (1)

- Standardization and simplification of antiretroviral regimens and monitoring tools (facilitate initial treatment)

- Better definition of first- and second-line regimens
  - First line: regimens based on non-nucleoside reverse transcriptase inhibitors (five drugs and four possibilities)
  - Second line: regimens based on protease inhibitors (preferentially protease inhibitor boosted)

- Fixed-drug combinations and co-blister packs to improve adherence, limit emergence of drug resistance and facilitate logistics

Scaling up antiretroviral therapy in resource-limited settings - Key elements (2)

- Stavudine, lamivudine and nevirapine (d4T/3TC/NVP) is the most suitable first-line option for immediate start in very-low-resource settings (no laboratory, low cost, fixed-drug combinations available, suitable for different patient groups)

- Body weight, total lymphocyte count, haemoglobin colour scale, objective monitoring parameters (CD4 desirable, viral load not recommended)

- Symptom-directed laboratory evaluation of toxicity

Assessing eligibility for antiretroviral therapy

- Laboratory-confirmed HIV infection

- Clinical assessment of HIV infection and HIV disease (WHO staging system)

- Assessment of CD4 cell count

- Total lymphocyte count as a substitute indication for treatment (symptomatic HIV disease stage II)

- Assessment of viral load not considered necessary to start therapy
WHO clinical stage 1: asymptomatic
- No weight loss
- No symptoms or only persistent generalized lymphadenopathy
- Performance scale 1: asymptomatic, normal activity

WHO clinical stage 2: mild disease
- Weight loss 5-10%
- Minor mucocutaneous manifestations, herpes zoster within past five years, recurrent upper respiratory infections (bacterial sinusitis or otitis)
- Performance scale 2: symptomatic, normal activity

WHO clinical stage 3: moderate disease
- Weight loss >10%
- Unexplained chronic diarrhea or unexplained prolonged fever >1 month, oral candidiasis (thrush), oral hairy leukoplakia, pulmonary TB within last year, severe bacterial infections (such as pneumonia or pyomyositis)
- Performance scale 3: bedridden <50% of the day during past month

WHO clinical stage 4: severe disease (AIDS)
- HIV wasting syndrome
- Pneumocystis carinii pneumonia, toxoplasmosis of the brain, Cryptosporidium diarrhea >1month, extrapulmonary cryptosporidiosis, cytomegalovirus disease other than liver, spleen or lymph node (that is, retinitis), mucocutaneous or visceral herpes simplex virus infection, progressive multifocal leukoencephalopathy, any disseminated endemic mycosis, candidiasis of esophagus, trachea, bronchi, atypical Mycobacterium tuberculosiis TB (disseminated or lungs), non-typhoid Salmonella septicemia, extrapulmonary TB, lymphoma, Kaposi’s sarcoma, HIV encephalopathy
- Performance scale 4: bedridden > 50% of the day during past month

Recommendations for initiating antiretroviral therapy among adults and adolescents with documented HIV infection (1)
If CD4 assay available:
- WHO stage IV disease, irrespective of CD4 count
- WHO stage III disease, consider using CD4 count <350 to assist decision-making
- WHO stage I or II if CD4 count <200

Recommendations for initiating antiretroviral therapy among adults and adolescents with documented HIV infection (2)
If CD4 assay not available:
- WHO stage IV disease, regardless of total lymphocyte count
- WHO stage III disease, regardless of total lymphocyte count
- WHO stage II or I disease with total lymphocyte count <1200

Antiretroviral regimens and monitoring
- WHO-recommended first- and second-line antiretroviral regimens and issues considered for selection
- Steps recommended for clinical and laboratory monitoring of antiretroviral therapy
Considerations that informed the choice of first-line antiretroviral regimens

- Potency
- Side-effect profile
- Maintenance of future options
- Predicted adherence
- Availability of fixed-dose combinations (FDCs) of antiretroviral drugs
- Coexistent medical conditions (TB and pregnancy or a risk thereof)
- Concomitant medications
- Presence of a resistant viral strain
- Cost and availability
- Limited infrastructure
- Rural delivery

Current antiretroviral targets

Recommended ARVs

<table>
<thead>
<tr>
<th>Nucleoside Reverse Transcriptase Inhibitors (NRTIs)</th>
<th>Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)</th>
<th>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</th>
<th>Protease Inhibitors (Pis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>Tenofovir</td>
<td>Nevirapine</td>
<td>Saquinavir</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Lamivudine</td>
<td>ZDV</td>
<td>NVP</td>
</tr>
<tr>
<td>Stavudine</td>
<td>d4T</td>
<td>ddI</td>
<td>SQV</td>
</tr>
<tr>
<td>Abacavir</td>
<td>3TC</td>
<td>lamivudine (3TC)</td>
<td>RTV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lopinavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nelfinavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NFV</td>
</tr>
</tbody>
</table>

WHO-recommended first and second-line antiretroviral therapy regimens for children

<table>
<thead>
<tr>
<th>First-line regimen</th>
<th>Second-line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>stavudine (d4T) or zidovudine (ZDV)</td>
<td>abacavir (ABC)</td>
</tr>
<tr>
<td>+ lamivudine (3TC)</td>
<td>+ didanosine (ddI)</td>
</tr>
<tr>
<td>nevirapine (NVP)</td>
<td>+ protease inhibitor: lopinavir with a ritonavir boost (LPV/r) or nelfinavir (NFV), or saquinavir with a ritonavir boost (SQV/r) if weight &gt;25 kg</td>
</tr>
</tbody>
</table>

Problems with second-line antiretroviral regimens

- Multiple resistance mutations
- High pill burden
- Limited experience
- Availability of tenofovir (TDF)
- Hypersensitivity to abacavir (ABC)
- Cold chain for ritonavir (RTV)
- High cost

First-line antiretroviral regimens

- Tenofovir 300 or 360 mg once or twice daily
- Lamivudine 150 mg once daily
- Efavirenz 600 mg once daily

*Insufficient pharmacokinetic data on tenofovir in children to recommend it as an alternative nucleotide reverse transcriptase inhibitor, and there are concerns about the bone toxicity of tenofovir
**Why fixed-drug combinations?**
- Significant reduction of daily tablet doses
- Improves adherence and reduces the risk of the emergence of resistance
- Lower cost
- Facilitates logistics
- Facilitates use of supervised treatment strategies
- Reduces the production process time, enabling accelerated delivery

**Fixed-dose combinations of antiretroviral drugs for use among HIV-positive adults and adolescents at the end of 2003**

**Three-drug fixed-dose combinations**
- Stavudine (30 mg) + lamivudine (150 mg) + nevirapine (200 mg)*
- Stavudine (30 mg) + lamivudine (150 mg) + nevirapine (200 mg)*
- Zidovudine (300 mg) + stavudine (150 mg) + nevirapine (200 mg)
- Zidovudine (300 mg) + lamivudine (150 mg) + nevirapine (200 mg)

**Two-drug fixed-dose combinations** (for use with a third antiretroviral drug and for nevirapine lead-in dosing)
- Stavudine (30 mg) + lamivudine (150 mg)
- Stavudine (40 mg) + lamivudine (150 mg)
- Zidovudine (300 mg) + lamivudine (150 mg)

*Presentations with WHO prequalified manufacturers.

**Special considerations among people with TB**
- Rifampicin drug interactions with nevirapine and protease inhibitors
- Pill burden and adherence
- Drug toxicity
  - First-line recommendation: zidovudine or stavudine + lamivudine + efavirenz (600 or 800 mg/day)
  - Use of nevirapine questioned: increased liver toxicity? Poor efficacy due to 50% reduction in serum concentrations?
  - Zidovudine + lamivudine + abacavir is another alternative, especially in children
- The optimal time to start antiretroviral therapy among people with TB is unknown, but based on expert consensus:
  - CD4 <200: start TB therapy; recommend antiretroviral therapy as soon as TB therapy is tolerated (2–8 weeks)
  - CD4 200–350: start TB therapy; consider antiretroviral therapy
  - CD4 >350: start TB therapy; defer antiretroviral therapy
- If no CD4 available: start TB therapy; recommend antiretroviral therapy, timing based on other clinical signs of immunodeficiency

**Clinical and laboratory assessment of adults and adolescents on antiretroviral therapy**

**Evaluations at baseline:**
- HIV disease stage
- Concomitant health conditions (TB, pregnancy, major mental disorder)
- Concomitant medication use (including traditional therapies)
- Body weight
- Patient readiness for therapy

**Evaluations while on therapy:**
- Assessment for signs and symptoms of potential drug toxicity
- Body weight
- Assessment of response to therapy
- Assessment of adherence
- Laboratory evaluation when clinically indicated (depends on the antiretroviral drug regimen in use)
**Basic laboratory monitoring for first-line antiretroviral regimens at community or district centre (levels 1 & 2)**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Laboratory test at baseline</th>
<th>Laboratory test on therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>stavudine + lamivudine + nevirapine</td>
<td>Not required (CD4 desirable)</td>
<td>Symptom directed; haemoglobin, white blood cells, CD4 every 6–12 months if available</td>
</tr>
<tr>
<td>zidovudine + lamivudine + nevirapine</td>
<td>Desirable but not required (CD4 and pregnancy test desirable)</td>
<td>Symptom directed; haemoglobin, complete blood count, CD4, pregnancy test</td>
</tr>
<tr>
<td>stavudine + lamivudine + efavirenz</td>
<td>Not required (CD4 and pregnancy test desirable)</td>
<td>Symptom directed; haemoglobin, complete blood count, CD4, pregnancy test</td>
</tr>
<tr>
<td>zidovudine + lamivudine + efavirenz</td>
<td>Desirable but not required (CD4 and pregnancy test desirable)</td>
<td>Symptom directed; haemoglobin, complete blood count, CD4, pregnancy test</td>
</tr>
</tbody>
</table>

*Obtain if symptoms of toxicity develop (not routine).*

**Recommended tiered laboratory capabilities to monitor antiretroviral therapy**

<table>
<thead>
<tr>
<th>Community health centre (level 1)</th>
<th>District hospital (level 2)</th>
<th>Regional referral hospital (level 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid HIV test</td>
<td>Rapid HIV test</td>
<td>Rapid HIV test</td>
</tr>
<tr>
<td>Haemoglobin test (for zidovudine)</td>
<td>Second serological HIV rapid test method</td>
<td>Second serological HIV rapid test method</td>
</tr>
<tr>
<td>Pregnancy test (for efavirenz in women)</td>
<td>Complete blood count and differential CD4 count ALT</td>
<td>Complete blood count and differential CD4 count Full chemistries</td>
</tr>
<tr>
<td>Sputum smear for TB (referral if microscopy not available)</td>
<td>Pregnancy test (for efavirenz in women)</td>
<td>Pregnancy test (for efavirenz in women)</td>
</tr>
<tr>
<td>Sputum smear for TB</td>
<td>Sputum smear for TB</td>
<td>Viral load testing</td>
</tr>
</tbody>
</table>

**Haemoglobin colour scale: a simple, practical and inexpensive tool developed by WHO**

**Mean viral load, CD4 and weight evolution after antiretroviral therapy in South Africa (MSF project)**

**Clinical and CD4 definition of treatment failure in adults and adolescents**

<table>
<thead>
<tr>
<th>Clinical criteria</th>
<th>CD4 criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• New opportunistic infection or malignancy (must differentiate from immune reconstitution syndrome)</td>
<td>• Recurrence of prior opportunistic infection (such as oral candidosis refractory to treatment)</td>
</tr>
<tr>
<td>• Recurrence of prior opportunistic infection (such as oral candidosis refractory to treatment)</td>
<td>• Onset or recurrence of WHO stage III conditions</td>
</tr>
<tr>
<td>• Onset or recurrence of WHO stage III conditions</td>
<td>• Return CD4 cell count to pre-therapy baseline or below without other cause</td>
</tr>
<tr>
<td>• ≥50% fall from peak CD4 count on therapy without other cause</td>
<td></td>
</tr>
</tbody>
</table>

*Recurrence of TB may not reflect progression as reinfection may occur; clinical evaluation necessary.*

**Immune reconstitution**

- **Inflammatory response in first 1–2 months**
- **Clinical spectrum** – fever, lymph node swelling, lung and central nervous system involvement
- **With latent Mycobacterium tuberculosis infection**, can develop active TB
- **If active TB develops**, it is not necessary to stop antiretroviral therapy.
Correlation between adherence and viral failure


People with viral failure (%)
P = 0.00001, r = –0.55

Adherence (%)

>95 90–95 80–90 70–80 <70

HIV resistance: underlying concepts

- Genetic variants are continuously produced as a result of high viral turnover and inherent error rate of reverse transcriptase.
  - Mutations at each codon site occur daily.
  - Survival depends on replication competence and presence of drug or immune selective pressure.
  - Double mutations in same genome also occur, but three or more mutations in the same genome is a rare event.
  - Numerous natural polymorphisms exist.

HIV drug resistance and developing countries

- The induction and spread of drug-resistant strains is an inevitable consequence of the introduction of antiretroviral therapy.
- This is not a reason to delay the introduction of effective therapy into developing countries.
- Strategies to prevent drug resistance should be introduced in parallel with antiretroviral therapy programmes.
- Drug resistance monitoring should be an essential component of antiretroviral therapy programmes.
- Technical issues need to be faced
  - Assay questions
  - Technology transfer

Adverse effects of antiretroviral drugs: class-specific effects

NsRTI  Lactic acidosis Mitochondrial toxicity
        Lipodystrophy syndrome with long usage
NtRTI   Mitochondrial toxicity
NNRTI   Skin rash
        Lipodystrophy syndrome
        Hyperlipidaemia
        Hyperglycaemia
PI      Hepatitis
        Lipodystrophy syndrome
        Hyperlipidaemia
        Hyperglycaemia

Specific drug side-effects

- **Zidovudine**: gastrointestinal intolerance, haematotoxicity (anaemia), muscle pains, headache
- **Stavudine**: peripheral neuropathy, pancreatitis, lipoatrophy
- **Nevirapine**: cutaneous hypersensitivity, hepatotoxicity
- **Efavirenz**: teratogenicitiy, mental disorder
- **Nelfinavir**: gastrointestinal intolerance, skin rash
- **Lopinavir**: gastrointestinal intolerance, hypercholesterolaemia and triglyceridaemia
**First-line antiretroviral regimens: major side effects**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Major side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine + lamivudine + nevirapine</td>
<td>Anaemia; skin and liver toxicity; cannot use nevirapine with rifampicin</td>
</tr>
<tr>
<td>Zidovudine + lamivudine + efavirenz</td>
<td>Anaemia; lipoatrophy and neuropathy; central nervous system symptoms and teratogenicity</td>
</tr>
</tbody>
</table>

**Simplified guidelines for antiretroviral therapy**

**First-line regimen (HIV-1 infection)**

- **d4T/3TC/NVP**
  - If clinical hepatitis: Replace ZDV with d4T and EFV
  - If severe rash: Replace NVP with EFV
  - If neuropathy or pancreatitis: Replace d4T with ZDV
  - If severe anaemia: Replace NVP with EFV

**Second-line regimen (HIV-1 infection)**

- **TDF + d4T + LPV/r**
  - If severe dyslipidaemia: Replace LPV/r with SQV/r
  - If severe gastrointestinal intolerance: Replace d4T with ABC

**First-line regimen (HIV-2 infection)**

- **d4T/3TC/NFV**
  - If severe gastrointestinal intolerance: Replace NFV with SQV/r

**Second-line regimen (HIV-2 infection)**

- **TDF + d4T + LPV/r**
  - If severe dyslipidaemia: Replace LPV/r with SQV/r
  - If severe gastrointestinal intolerance: Replace d4T with ABC
Document 6.4

Introduction to the exercise for Unit 6

For this exercise, your facilitator will divide the participants into groups of three. The purpose of the exercise is to analyze the provision of antiretroviral therapy services in Fictitia, identify gaps and propose activities to address these gaps.

- Read pages 140-148 in the report from Fictitia in Annex 1.

- Analyse what the national HIV/AIDS programme has done so far in the country in relation to WHO recommendations for a public health approach, with special focus on:
  1) eligibility for antiretroviral therapy;
  2) the skills available through the health system for delivering antiretroviral therapy services;
  3) the capacity of the laboratory network to comply with the requirements for antiretroviral therapy monitoring; and
  4) the management of people coinfected with TB/HIV.

- Identify gaps in the programme (especially in terms of strengthening the capacity of the health system) and propose priorities for your planning.

- Prepare to present the group work in the plenary session.

Tell a facilitator when you are ready for the plenary discussion.
Unit 7: Drug management for controlling TB and HIV/AIDS

Objectives

By the end of this unit, participants will be able:
1) to discuss the various aspects of TB and HIV drug management using a logical framework;
2) to identify the differences between the procurement practices for TB and HIV/AIDS drugs; and
3) to identify gaps and priorities in the procurement of TB and HIV/AIDS drugs and to propose solutions to facilitate drug management in implementing collaborative TB/HIV activities.

Methods

Plenary presentation: Drug management for controlling TB and HIV/AIDS
Exercise
Plenary discussion

Materials

Document 7.1: Drug management for controlling TB and HIV/AIDS (slides)
Document 7.2: Exercise
Drug management for controlling TB and HIV/AIDS

Document No. 7.1

TB/HIV course for managers at the national and subnational levels

Objectives of the unit

• To discuss the various aspects of TB/HIV drug management using a logical framework
• To identify the differences between procurement practices for TB and HIV/AIDS drugs
• To identify gaps and priorities in procurement of TB and HIV/AIDS drugs and to propose solutions to facilitate the implementation of collaborative TB/HIV activities in drug management

Pharmaceutical management cycle

Pharmaceutical management is the set of practices aimed at ensuring the timely availability and appropriate use of safe, effective and high-quality medicines and related products and services in any health care setting

Standardized treatment regimens and uninterrupted drug supply are basic principles of the DOTS Strategy

• Political commitment to programme, including normative, financial, planning, surveillance, training and supervision functions
• Case detection among people presenting with symptoms, using low-cost tools
• Standardized treatment with direct observation
• System for uninterrupted supply of high-quality TB drugs
• Recording and reporting system allowing accountability and outcome evaluation
TB drug supply

- There are key rules for estimating drug needs (based on previous consumption and/or on notifications)
- Regimens are standardized
- Fixed-drug combinations and/or blister packs are recommended
- The cost of one first-line regimen is about US$ 15
- The Global Drug Facility (GDF) is fully operational to support the procurement of quality drugs at the lowest possible price
- Low-cost second-line drugs are available for Green Light Committee (GLC) programmes

Management of HIV supplies Key principles

- HIV-related drugs and diagnostics are ordinary supplies, but …
  - Treatment is for life, and treatment interruptions (supply interruptions) have to be avoided at all cost.
  - The supply system has to cater for the various treatment regimens and the changing proportions to which these are used over time.
  - Antiretroviral drugs are relatively expensive and in high demand.
  - Antiretroviral therapy receives high-level government and donor support and scrutiny.
  - Antiretroviral drugs and test kits may require cold storage and often have short shelf lives.

Selection

- National consensus: a committee + guidelines (regimen, weight band, strength, loose or combined, box or blister or kit)
- Curative drugs: antiretroviral drugs, opportunistic infections, palliative care, AIDS-related cancer, opioid dependence
- Preventive drugs: isoniazid, co-trimoxazole
- HIV diagnosis kit
- CD4, viral load and drug resistance equipment

Notes:
- More people need to change regimens for HIV/AIDS (because of failure or side-effects) than for TB (10% versus 2%)
- Recommendations to shift from first- to second-line standardized for TB but are under constant revisions for antiretroviral drugs

Procurement: quantification

- Fixed number of people receiving antiretroviral therapy per year
- Previous antiretroviral consumption times 2 – existing stock
- Previous activity: number of people receiving antiretroviral therapy times number of drugs per year times 2 – existing stock
- Morbidity: HIV prevalence rate times the population covered

Notes:
- Isoniazid preventive therapy must be quantified
- Number of HIV/AIDS cases is harder to predict than for TB, as quarterly TB reporting is systematized
- Lack of expertise for appropriate quantification of antiretroviral drugs during scaling-up (unlike TB drugs)
- Antiretroviral drugs and test kits have short shelf lives (eight months)
- Complex procurement due to multiple sources of funds
- Manufacturers and suppliers unable to meet demand (shortages of stavudine and efavirenz)

Distribution

- Port clearing (document, testing and taxes)
- Storage: separate versus common, bulk versus shelves, expiry dates, temperature and accountability (register and bin card)
- Push or pull system (consumption, activity and order forms)
- Transport (frequency, separate versus common)

Notes:
- Small but sufficient stock to avoid expiry at the local level
- Coordinated TB/HIV drug distribution based on model used
- Security for antiretroviral drugs (more expensive) is a priority
- Cold chain needed for some antiretroviral drugs

Use

- Health unit provider or home delivery (by health staff)
- Drug provision (daily, weekly or monthly)
- Adherence
  - Recording (patient card, register and report)
  - DOT, weekly observation
  - Blister, kit or combined tablets
  - Patient education and support (psychological)
  - Patient cost (free of charge, contribution or unofficial)

Notes:
- Antiretroviral therapy is more expensive for families and programmes than TB (tests, drugs and programme)
- Continuous (lifetime) motivation necessary for antiretroviral therapy
- Accurate training on side-effects for Antiretroviral drugs necessary
- Irrational use of antiretroviral drugs leads to greater wasting of resources
- Lack of expertise in managing antiretroviral therapy and formulations for children
Procurement: tender

- Open tender: too long
- Restricted tender: market information on price and quality:
  - www.who.int/medicines, www.accessmed-msf.org
    - Prequalified products: "Access to HIV/AIDS drugs and diagnosis of acceptable quality" January 2004
    - Indicative price: "Sources and prices of selected medicines and diagnosis for people living with HIV/AIDS" June 2003
    - Untangling the web of price reductions, December 2003
- Selected tender: national manufacturer or supplier, patented or generic

Procurement: generic versus originator (1)

- Doha Declaration 2001 (TRIPS and public health)
  - Flexibility, such as compulsory licensing, is introduced to ensure that the TRIPS Agreement does not prevent members from taking measures to protect public health.
- Government can allow companies to make patented product under licence without the consent of the patent owner for the domestic market (antiretroviral drugs only)

Procurement: generic versus originator (2)

WTO member government decision of 30 August 2003: the DOHA Declaration effectively limited the ability of countries that cannot make pharmaceutical products from importing cheaper generics from countries where pharmaceuticals are patented.

The decision allows any member country to export pharmaceutical products made under compulsory license.

Twenty-three countries announced that they would voluntarily refrain from using the system for import.

Making commodities available for countries: the WHO AIDS Medicines and Diagnostics Service

Group of partners
- United Nations agencies
  - WHO (EDM, EHT, CPS and Essential Drugs units and HIV regional advisors in regional offices), UNICEF, World Bank, UNAIDS, UNFPA, UNDP
- Technical organizations and donor agencies
- Observers
  - MSF, United States Department of State (President’s Emergency Plan for AIDS Relief), United States Agency for International Development
- Secretariat
  - AMDS unit of Department of HIV/AIDS of WHO

What the AMDS offers

- Governments, NGOs: intelligence for making informed choices on procurement (prices of drugs and diagnostics and information on regulations and intellectual property rights)
- Governments, NGOs: capacity-building for managing procurement and supply
- Manufacturers: information necessary for forecasting volumes to be produced (not yet available)

What the AMDS can provide to countries

- Technical country support for the pharmaceutical management cycle
- Guidance on selection of core antiretroviral drugs.
- Guidance on legal issues related to importing generic medicines
- Prequalification of drugs and diagnostics
- Information on product specification to be used in tenders
- Guidance and training in local production and quality assurance
Document 7.2

Introduction to the exercise for Unit 7

For this exercise, your facilitator will divide the participants into groups of three. The purpose of the exercise is to estimate the antiretroviral therapy and TB services needed in a given country or region, to identify gaps and propose activities to address these gaps.

• Select one specific country (or a region within the country) representing the group members.

• Provide figures (or estimates) on:
  1) the number of people infected with HIV and coinfected with TB and HIV living in the country (or region);
  2) the number of people eligible for antiretroviral therapy in the country (or region) and the number of people requiring TB treatment and isoniazid preventive therapy;
  3) the number of people infected with HIV and coinfected with TB and HIV currently receiving antiretroviral therapy, TB treatment regimen and isoniazid preventive therapy in the country (or region);
  4) the target year for universal access to antiretroviral therapy in the country (or region);
  5) the number of people receiving antiretroviral therapy at the end of the year in the country (or region); and
  6) the number of people receiving isoniazid preventive therapy at the end of the year in the country (or region).

• Discuss the figures or estimates.

• List three priority interventions to improve the pharmaceutical management cycle to achieve universal access to antiretroviral therapy in the country (or region).

• Prepare to present the group work in the plenary session.

Tell a facilitator when you are ready for the plenary discussion.
Unit 8: The Interim policy on collaborative TB/HIV activities

Objectives

By the end of this unit, participants will be able:
1) to describe the main elements of the interim policy on collaborative TB/HIV activities; and
2) to discuss the main problems, constraints and opportunities found in implementing collaborative TB/HIV activities at the country level.

Methods

Plenary presentation: The *Interim policy on collaborative TB/HIV activities*
Exercise
Plenary discussion

Materials

Document 8.1: The Interim policy on collaborative TB/HIV activities (slides)
Document 8.2: Exercise
Document 8.3: *Interim policy on collaborative TB/HIV activities* (6)
Document 8.4: *Guidelines for implementing collaborative TB and HIV programme activities* (7)
Document 8.5: *Strategic framework to decrease the burden of TB/HIV* (8)
Document 8.1

The Interim policy on collaborative TB/HIV activities
Document No. 8.1

TB/HIV course for managers at the national and subnational levels

Objectives of the unit

- To describe the main elements of the interim policy on collaborative TB/HIV activities
- To discuss the main problems, constraints and opportunities found in implementing collaborative TB/HIV activities at the country level

Background on AIDS and ProTEST

- 1981 AIDS reported in the United States
- 1984 AIDS in Africa
- 1984 TB in AIDS
- 1989+ Descriptive studies of HIV and TB
- 1991 Thiacetazone and HIV
- 1992 HIV-related mortality, relapse and morbidity in TB
- 1997 ProTEST and other projects conceived
- 2000 Interventions defined

ProTEST

- WHO initiative to promote testing for HIV using voluntary counselling and testing as an entry point to a range of prevention and care interventions related to TB/HIV and sexually transmitted infections
- Objective of ProTEST:
  To develop a more cohesive response to TB in settings with high HIV prevalence through collaboration between TB and HIV control programmes.

ProTEST

Interventions:

- Collaboration between stakeholders and the health service
- Improved access to high-quality voluntary counselling and testing
- Intensified case-finding and treatment of active TB among people living with HIV/AIDS
- Isoniazid preventive therapy to treat latent TB
- Co-trimoxazole preventive therapy to reduce morbidity and mortality from opportunistic infections
- HIV prevention (including condoms and management of sexually transmitted infections)
- Improved clinical care for people living with HIV/AIDS

Results:

- TB/HIV collaboration was feasible
- Improved human resources capacity
- Increased access to high-quality voluntary counselling and testing (VCT) services
- Improved TB case-finding
- Isoniazid preventive therapy (IPT) and co-trimoxazole preventive therapy (CPT) introduced
- HIV prevention activities introduced or enhanced
- Community involvement developed
- Profile of TB/HIV raised
ProTEST

Lessons learned:
- Involvement of all stakeholders is critical
- Additional staff are essential
- Technical support is essential
- More operational research and cultural understanding are required to increase adherence to preventive treatments
- Standard monitoring and evaluation tools are needed
- Joint TB/HIV work sets stage for antiretroviral therapy

Rationale for joint TB/HIV activities
- HIV drives TB incidence and mortality in areas with a high HIV prevalence: 11–50% of people living with HIV/AIDS die from TB
- DOTS alone is insufficient to control TB in these areas
- Joint TB/HIV interventions, jointly delivered, are needed to control HIV-associated TB, expand DOTS and control HIV
- TB control system can be a major partner for delivery of antiretroviral therapy and thus for “3 by 5”, the United States President’s Emergency Plan for AIDS Relief etc.

TB is not just part of the problem; it is also part of the solution

Principles
- “Two diseases, one patient”
  - Patient focuses in care delivery for both diseases at the same time
- There is an ongoing catastrophe, therefore:
  - No more “projects”
  - Immediate scale up of what works
  - Revise as more evidence becomes available
- No separate programme
  - Collaborative activities add to existing strategies for controlling TB and HIV/AIDS
- Policy needs to be global

Sequence of TB/HIV policy development
- Builds on field experience with ProTEST (Malawi, South Africa and Zambia) and other TB/HIV pilot projects (Botswana, Cote d’Ivoire, Kenya, Rwanda, Thailand, etc.)
- Complements the Strategic framework to decrease the burden of TB/HIV, which provides a complete rationale and mentions what could be done
- Complements the Guidelines for implementing collaborative TB and HIV programme activities, which show how to organize at the national and district levels

The Interim policy on collaborative TB/HIV activities states what countries should do

Process for the interim policy
- Under the auspices of the Global TB/HIV Working Group
- Iterative drafting process by:
  - technical experts from TB and HIV
  - health management policy-makers,
  - people living with HIV/AIDS and their advocates,
  - international and national TB and HIV programme managers and donor agencies

Goal and objectives
Goal
To decrease the burden of TB and HIV in dually affected populations

Objectives
A. to establish the mechanisms for collaboration between TB and HIV/AIDS programmes
B. to decrease the burden of TB among people living with HIV/AIDS
C. to decrease the burden of HIV in Tuberculosis patients
Collaborative TB/HIV activities

A. Establish mechanisms for collaboration
   1. Set up coordinating bodies for TB/HIV activities at all levels
   2. Conduct surveillance of HIV prevalence among tuberculosis patients
   3. Carry out joint TB/HIV planning
   4. Conduct monitoring and evaluation

B. Decrease the burden of TB among people living with HIV/AIDS
   1. Establish intensified TB case-finding
   2. Introduce isoniazid preventive therapy
   3. Ensure TB infection control in health care and congregate settings

C. Decrease the burden of HIV among tuberculosis patients
   1. Provide HIV testing and counselling
   2. Introduce HIV prevention methods
   3. Introduce co-trimoxazole preventive therapy
   4. Ensure HIV/AIDS care and support
   5. Introduce antiretroviral therapy

Thresholds for collaborative TB/HIV activities

<table>
<thead>
<tr>
<th>Category</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| **Category I**  
Countries with national adult HIV prevalence rate ≥1%  
OR  
Countries in which national HIV prevalence among tuberculosis patients is ≥5%. | Implement all recommended collaborative TB/HIV activities |

<table>
<thead>
<tr>
<th>Category II</th>
<th>Implement all recommended collaborative TB/HIV activities in administrative areas with HIV prevalence ≥ 1% and in other areas as in Category III</th>
</tr>
</thead>
</table>
| Countries with national adult HIV prevalence rate below 1%  
AND  
Administrative areas that have adult HIV prevalence rate ≥1% | |

| Category III | HIV surveillance among TB patients  
Activities to decrease the burden of TB in people living with HIV/AIDS (with special emphasis on high HIV risk groups) |
Targets for collaborative TB/HIV activities

- By 2005, all category I and II countries will have established at least a national TB/HIV coordinating body.
- By 2007, all category I and II countries will have developed joint TB/HIV implementation plans.
- By 2007, all category I and II countries will have established a system for HIV surveillance among TB patients.

Keep in mind:

- It is high time for TB and HIV/AIDS programmes to work together
- Much synergy is possible
- Many missed opportunities would be prevented
- Universal access to antiretroviral therapy, Stop TB strategy and other approaches and initiatives provide many opportunities for TB/HIV collaboration – we must take advantage of them
Introduction to the exercise for Unit 8

For this exercise, your facilitator will divide the participants into four groups. The purpose of the exercise is to review in detail the activities proposed in the *Interim policy on collaborative TB/HIV activities*.

- Each group is assigned three or four activities from the *Interim policy on collaborative TB/HIV activities* as follows:
  - Group 1: A1; B2; B3; C5;
  - Group 2: A2; B1; C4;
  - Group 3: A3, C3; and
  - Group 4: A4; C1; C2.

- Familiarize yourself with the assigned activities.

- Discuss within the group and provide an example of how each of the assigned activities could be implemented in one of the countries or regions represented in the group.

- Brainstorm within the group on the constraints and opportunities found in implementing collaborative TB/HIV activities at the country level.

- Prepare to present the group work in the plenary session.

**Tell a facilitator when you are ready for the plenary discussion.**
Unit 9: Recording and reporting for the implementation of collaborative TB/HIV activities

Objectives

By the end of this unit, participants will be able:
1) to describe how recording and reporting is organized for controlling TB;
2) to describe how recording and reporting is organized for controlling HIV/AIDS; and
3) to discuss relevant country experiences on TB/HIV recording and reporting and how existing recording and reporting systems can be harmonized to serve the implementation of collaborative TB/HIV activities.

Methods

Plenary presentations: Recording and reporting for controlling TB and HIV/AIDS
Plenary discussion

Materials

Document 9.1: Recording and reporting for controlling TB (slides)
Document 9.2: Recording and reporting for controlling HIV/AIDS (slides)
Document 9.3: TB and HIV/AIDS forms (handout)
Document 9.1

Recording and reporting for controlling TB

Document No. 9.1

TB/HIV course for managers at the national and subnational levels

Objectives of the presentation

- To describe how recording and reporting are organized for controlling TB
- To discuss relevant country experiences on TB/HIV recording and reporting and how existing recording and reporting systems can be harmonized to serve the implementation of collaborative TB/HIV activities

TB determinants and case definitions

Core package for TB recording and reporting

Core package for TB recording and reporting

Indicators for analysing TB case-finding
Indicators for analysing TB treatment results

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Calculation</th>
<th>Some possible interpretations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear conversion rate (percentage)</td>
<td>New pulmonary TB+ in one quarter a who became negative after intensive phase treatment times 100</td>
<td>Less than 85%: absence of follow-up sputum smear examination, poor DOT, excess of deaths and transfers out, poor investigation about previous TB treatment, drug resistance or poor reporting</td>
</tr>
<tr>
<td></td>
<td>New pulmonary TB+ registered in the same quarter</td>
<td></td>
</tr>
<tr>
<td>Cure rate (percentage)</td>
<td>New pulmonary TB+ cured in one quarter b times 100</td>
<td>Less than 85% cure: as above</td>
</tr>
<tr>
<td></td>
<td>New pulmonary TB+ registered in the same quarter</td>
<td></td>
</tr>
<tr>
<td>Programme success rate (percentage)</td>
<td>New pulmonary TB+ in one quarter cured and completed treatment c times 100</td>
<td>Less than 85% (target for TB control): poor overall programme performance</td>
</tr>
<tr>
<td></td>
<td>New pulmonary TB+ registered in the same quarter</td>
<td></td>
</tr>
</tbody>
</table>

a The same is applied to relapse of pulmonary TB+. b The same is applied to other treatment result rates in new pulmonary TB+ and relapse pulmonary TB+. c The same is applied to calculate the other rates in new pulmonary TB+ and relapse pulmonary TB+.

Cohort analysis

In a race: ➔

A group of people start together a 10-km foot race

How many people completed the race?

In a TB programme:

A group of people with TB disease start treatment within one quarter

How many patients completed this treatment?

Results expected in a good TB programme

- Success rate >85%
- Death rate <5%
- Unsatisfactory outcomes (default or failure) <10%

TB forms and HIV/AIDS (1)

Additional information that will have to be captured in TB recording and reporting forms:
- Offered HIV test
- Counselling and tested
- Test result positive or negative
- Given co-trimoxazole
- Referred for HIV care and support
- Given antiretroviral therapy during or at the end of TB treatment

TB forms and HIV/AIDS (2)

- Main issue: confidentiality of HIV test results in the TB register.
- The response: the TB register already contains confidential patient information that should be treated with the same level of confidentiality as HIV results.
- The solution is not to hide HIV results but rather to improve the confidentiality of the TB register.
Recording and reporting for controlling HIV/AIDS

Document No. 9.2

TB/HIV course for managers at the national and subnational levels

Objectives of the presentation

• To describe how recording and reporting is organized for controlling HIV/AIDS

• To discuss relevant country experiences on TB/HIV recording and reporting and how existing recording and reporting systems can be harmonized to serve the implementation of TB/HIV collaborative activities

Patient tracking data serve multiple needs

• Direct patient care
  - Clinical team caring for group of patients
  - Facilitates shift from acute to chronic care
• Monitoring drug supply and preparing facility drug orders
• Summarizing and reporting data to meet district and national programme needs and to track progress to targets

Patient tracking, once established
Data collection

Contribution of patient tracking to the milestones on universal access to antiretroviral therapy

<table>
<thead>
<tr>
<th>Level of monitoring and evaluation</th>
<th>Milestone</th>
<th>Data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>9. Children, women and men with advanced HIV receiving antiretroviral therapy</td>
<td>Country reports, site reporting, industry, nongovernmental organizations; patient tracking – current on antiretroviral therapy (numerator), once established</td>
</tr>
<tr>
<td></td>
<td>11. Survival on antiretroviral therapy</td>
<td>Patient tracking, once established</td>
</tr>
</tbody>
</table>

TB experience …

• Standardized treatment card
• Standardized register
• Globally standardized definitions
• Deliberately constrains the data collected
• Based on long experience
• Recently, new TB/HIV indicators
• Disease-specific (vertical)

HIV care (pre–antiretroviral therapy) register

To record data on:

• Patients’ data
• Date of HIV diagnosis
• Isoniazid prophylaxis
• Co-trimoxazole prophylaxis
• Fluconazole prophylaxis
• TB treatment
• Pregnancy
• Clinical staging system
• Outcome
  – antiretroviral therapy
  – lost to follow-up
  – death

Provides a link with antiretroviral therapy register:

• Date eligible
• Reason for eligibility
• Date eligible and ready
• Date antiretroviral therapy started
• Unique antiretroviral therapy number
Antiretroviral therapy register
(linked with pre-antiretroviral therapy register)

To record data on:
• Status when antiretroviral therapy starts
  – Clinical
  – Immune
• Isoniazid prophylaxis
• Co-trimoxazole prophylaxis
• TB treatment
• Pregnancy
• Antiretroviral therapy regimens
  – First line
  – Second line
  – Reason for change

Follow-up:
• Status at end of month
  – 24 months at least
• Functioning and CD4
  – 0, 6, 12 and 24 months

Consistent definitions for why an antiretroviral drug or regimen is changed

1. Toxicity or side-effects
2. Pregnancy
3. Risk of pregnancy
4. New TB
5. New drug available
6. Drug out of stock
7. Other reason (specify)
8. Clinical treatment failure
9. Immune failure
10. Viral failure

Consistent definitions
Follow-up status (outcomes)

• Alive and on antiretroviral therapy
  • Specify current regimen
• Alive and stopped antiretroviral therapy
• Alive and restart
• Lost (not the same as TB default)
• Dead
• Transfer in or transfer out with records

Consistent definitions for why antiretroviral therapy is stopped – reason codes

1 Toxicity or side-effects
2 Pregnancy – planned treatment interruption
3 Treatment failure
4 Poor adherence
5 Illness or hospitalization
6 Drug out of stock
7 Patient lacked financial resources
8 Other patient decision
9 Planned treatment interruption (record reason, such as early pregnancy)
10 Other

HIV care registers

Allow the measurement of:
• Medically eligible people
• Eligible and ready people
• Start of first-line therapy

Cohort analysis report:
Receiving antiretroviral therapy for 6 months, 12 months, yearly

• Proportion working, ambulatory or bedridden
• Proportion alive and receiving antiretroviral therapy at 6 and 12 months (survival indicator)
• Proportion still on a first-line regimen
• Proportion still on an original first-line regimen
• Proportion who have substituted an alternative first-line regimen
• Proportion switched to a second-line (or higher) regimen
• Median CD4 count (optional)
Cohort analysis report:
Receiving antiretroviral therapy for 6 months, 12 months, yearly

- Optional:
  - Reasons for switching regimen
  - Reasons for stopping

Malawi experience

Antiretroviral therapy patient master card
Every three months, update the register from the master card data

Antiretroviral therapy facility register
Every three months, perform quarterly cohort analysis from the updated register

Antiretroviral therapy patient cohort analysis
Every three months, each cohort is analysed for its treatment outcomes
[This allows survival analysis to be conducted]

Every three months, all the cohort case numbers and treatment outcomes are combined together
[This allows cumulative up-to-date data]

Antiretroviral therapy quarterly cohort analysis form

<table>
<thead>
<tr>
<th>NAME OF TREATMENT UNIT</th>
<th>Thyolo DH</th>
</tr>
</thead>
<tbody>
<tr>
<td>COHORT [specify the year and the quarter]</td>
<td>2003, Q2</td>
</tr>
<tr>
<td>Total number of patients initially registered in the cohort</td>
<td>116</td>
</tr>
<tr>
<td>Year in which evaluation is taking place</td>
<td>2003</td>
</tr>
<tr>
<td>Date on which evaluation is taking place</td>
<td>10 July</td>
</tr>
</tbody>
</table>

Of the total number registered in the cohort:
- Alive and on antiretroviral therapy: 106 (91%)
  - [Alive and on first-line regimen]: 101
  - [Alive and on alternative first-line regimen]: 5
  - [Alive and on second-line regimen]: 0
- Dead: 6
- Defaulted: 0
- Stopped: 4
- Transferred out to another treatment unit: 0

Of those alive:
- Ambulatory: 106
- At work: No information
- With side-effects: 14
- With pill count in bottle 8 or less: 63/63

(Note: pill count in bottle 8 or less is equivalent to 95% adherence)
Document 9.3

Course organizers will hand out the type of TB and HIV forms used in the country or area where the course is conducted.
Unit 10: Surveillance of HIV prevalence among people with TB disease

Objectives

By the end of this unit, participants will be able:

1) to describe surveillance of HIV prevalence among people with TB disease; and

2) to discuss the main problems, constraints and opportunities for implementing coordinated TB/HIV surveillance.

Methods

Plenary presentation: Surveillance of HIV prevalence among people with TB disease
Exercise
Plenary discussion

Materials

Document 10.1: Surveillance of HIV prevalence among people with TB disease (slides)
Document 10.2: Exercise
Document 10.3: *Guidelines for HIV surveillance among tuberculosis patients* (9)
Surveillance of HIV prevalence among people with TB disease

Objectives of the unit

- To describe surveillance of HIV prevalence among people with TB disease
- To discuss the main problems, constraints and opportunities for implementing coordinated TB/HIV surveillance

Guidelines for HIV surveillance among tuberculosis patients, 2nd edition

Why is surveillance of HIV prevalence among people with TB disease important?

- HIV prevalence among people with TB disease is a sensitive indicator for the spreading of HIV into the general population.
- Advocates increasing commitment to provide comprehensive HIV/AIDS care and support, including antiretroviral therapy, to HIV-positive people with TB disease.

Surveillance methods

The three main methods for surveillance of HIV among people with TB disease:

1. Data from routine patient care
2. Sentinel surveillance
3. Periodic (special) surveys

Surveillance methods for use in different HIV and TB prevalence settings

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
<th>Recommended surveillance method</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Countries with national adult HIV prevalence rate ≥1%</td>
<td>Routine testing plus Sentinel or special surveys to calibrate the results of routine testing</td>
</tr>
<tr>
<td>II</td>
<td>Countries with national adult HIV prevalence rate below 1% and HIV prevalence rate ≥5% in groups with high-risk behaviour</td>
<td>Routine testing or Sentinel or periodic surveys</td>
</tr>
<tr>
<td>III</td>
<td>Countries with national adult HIV prevalence rate below 1% and No population group with HIV prevalence rate ≥5%</td>
<td>Sentinel or periodic surveys if Routine testing not in use</td>
</tr>
</tbody>
</table>
Methods for measuring HIV prevalence among people with TB disease

<table>
<thead>
<tr>
<th>Surveillance method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Periodic (special) surveys</strong></td>
<td>Cross-sectional HIV sero-prevalence surveys among a sample of people with TB disease within a country. To include all newly registered TB cases, easier to focus on adult cases with smear-positive disease.</td>
</tr>
<tr>
<td><strong>Sentinel surveillance</strong></td>
<td>A predetermined number of people with TB disease are routinely tested at selected sentinel sites. People with TB disease are used as a sentinel group within a general HIV sentinel surveillance system. To include all newly registered TB cases, easier to focus on adult cases with smear-positive disease.</td>
</tr>
<tr>
<td><strong>Data from routine care</strong></td>
<td>Data collected from routine care of people with TB disease who are tested for HIV on a voluntary and confidential basis, through notification forms (TB or HIV/AIDS) or registers (TB, special TB + HIV), co-trimoxazole; isoniazid preventive therapy; voluntary counselling and testing; voluntary counselling and testing + TB) or cross-matching of HIV and TB notification systems (computerized).</td>
</tr>
</tbody>
</table>

**Ethical issues in HIV surveillance**
- An unlinked anonymous method is used to reduce bias caused by people refusing to be tested (based on testing blood drawn for other purposes).
- This is ethical only if it is both anonymous and unlinked. The ethical concern is that it limits access to antiretroviral therapy. All people with TB disease included in unlinked anonymous sero-prevalence surveys should have access to actively proposed, free, voluntary, confidential counselling and testing for HIV infection.
- If leftover blood not available, each person with TB should give informed consent. Alternatively, linked anonymous testing can be used in which only person with TB knows the result.
- Security and confidentiality policies and procedures in the transfer of information: minimal storage and retention of unnecessary or redundant paper or electronic reports; names removed from surveillance records when this no longer serves the public health purpose; records located in secure area; electronic data protected by coded passwords and computer encryption.

**Sentinel surveillance**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple and inexpensive</td>
<td>Possible conflict of responsibility</td>
</tr>
<tr>
<td>Focuses on easily accessible people</td>
<td>Problems if sample not taken routinely</td>
</tr>
<tr>
<td>Often part of a well-established HIV sentinel system</td>
<td>Ethical concerns</td>
</tr>
<tr>
<td>Good information on trends</td>
<td>Low representativity of sentinel sites</td>
</tr>
<tr>
<td>If poor testing, inconsistent results</td>
<td>Possible selection biases</td>
</tr>
</tbody>
</table>

**Methodological issues**

Use of sputum samples in HIV surveillance
- HIV tests other than on serum or blood (principally gingival secretions) are available and being further developed. In most countries sputum is routinely collected as part of the preliminary diagnostic investigations for all people with TB disease. In some settings this may favour the testing of sputum specimens over blood samples, especially if unlinked anonymous methods are followed (for example for sputum testing).
- The current sensitivity and specificity of HIV tests favours the use of blood testing over sputum testing. Even when unlinked methods are used, the current sensitivity and specificity of sputum testing methods (93.5–97.1% sensitivity and 99.7–100.0% specificity, respectively) are still not sufficiently high to avoid having a low positive predictive value (71.9%) in countries with low HIV prevalence (5%).
- Their use in HIV surveillance among people with TB disease is not recommended unless these tests have been validated in the country against gold-standard sero-HIV tests and found to be sufficiently reliable.
HIV testing from routine care

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Access to HIV prevention and care</td>
<td>• Need for large infrastructure (time, costs)</td>
</tr>
<tr>
<td>• Estimates the burden of HIV-related disease and demand for care</td>
<td>• If low coverage (&lt;80%) of testing, unreliable HIV prevalence estimates; if poor testing, inconsistent results</td>
</tr>
<tr>
<td></td>
<td>• May reflect more the access to health care services than the prevalence of HIV within the TB population</td>
</tr>
</tbody>
</table>

Data collection form for HIV prevalence surveys or sentinel surveillance among people with TB disease

- **Demographic data form**
  - Study site: ____________________________
  - Date of patient visit: _______ / _______ / _______ (dd/mm/yyyy)
  - Patient ID number: __________________
  - Age: __________ (years)
  - Sex: Male: [ ] Female: [ ]
  - Clinical presentation: Pulmonary: [ ] Extrapulmonary: [ ]
  - If relapse cases are included: New: [ ] Relapse: [ ]

- **Laboratory form**
  - Patient ID number: __________________
  - Results test 1: Positive: [ ] Negative: [ ] Doubtful: [ ] Not done: [ ]
  - Results test 2: Positive: [ ] Negative: [ ] Doubtful: [ ] Not done: [ ] (if undertaken)

Methodological issues

**Costs**

- Direct
  - Specimen collection equipment
  - Transport of specimens
  - Specimen testing kits
  - Laboratory staff time
  - Travel costs of staff
  - Costs of data entry and analysis
  - Dissemination of information (printing of reports, postage, presentations etc.)

- Indirect
  - Investment of staff time at all levels in activities, ranging from specimen collection to the overall coordination of surveillance activities

Challenges to TB/HIV surveillance

**Organizational and financial**

- Low awareness of importance: lack of political commitment to surveillance and insufficient investment
- Suffers from gaps in the TB/HIV initiative
- Lack of skilled epidemiological personnel
- Lack of feedback to those involved in surveillance activities

Concluding remarks

- HIV surveillance among people with TB disease is a key TB/HIV activity
- It should be part of a plan for joint TB/HIV activity with proper allocation of funds
- Surveillance methods in countries should vary according to the underlying HIV epidemic state and TB burden
- Considering ethical issues and any possible organizational constraints is important
- A guideline to provide a framework for this activity is now available
Document 10.2

Introduction to the exercise for Unit 10

For this exercise, your facilitator will divide the participants into four groups. The purpose of the exercise is to discuss how to implement surveillance of HIV among people with TB disease.

- Read pages 140-148 in the report on Fictitia in Annex 1.
- Review the available information on the epidemiological situation and surveillance system in Fictitia.
- Identify gaps in the surveillance component, in particular with relation to surveillance of HIV among people with TB disease, and propose priorities for addressing the gaps.
- Estimate the sample size and costs for a special survey to be conducted in Fictitia to estimate the prevalence of HIV among people with TB disease.
- Prepare to present the group work in the plenary session.

Tell a facilitator when you are ready for the plenary discussion.