

## CHAPTER 2

# Framework for effective control of drug-resistant tuberculosis

### 2.1 Chapter objectives

This chapter describes the five essential components of the framework approach to management of drug-resistant TB. It also introduces a systematic approach for tailoring these components to the local situation, with integration into a DOTS-based national TB control programme.

### 2.2 DOTS framework as applied to the management of drug-resistant tuberculosis

The framework is organized around the five components of the DOTS strategy because the underlying principles are the same (1–2):

- a. Sustained political commitment
- b. A rational case-finding strategy including accurate, timely diagnosis through quality-assured culture and DST
- c. Appropriate treatment strategies that use second-line drugs under proper case management conditions
- d. Uninterrupted supply of quality-assured antituberculosis drugs
- e. Standardized recording and reporting system

Each of these components involves more complex and costly operations than those for controlling drug-susceptible TB. However, addressing drug-resistant TB usually strengthens the national TB control programme.

#### 2.2.1 Sustained political commitment

Sustained political commitment is essential to establish and maintain the other four components. It requires both long-term investment and leadership to ensure an appropriate environment for integrating the management of drug-resistant TB into national TB control programmes. An appropriate environment includes adequate infrastructure, development and retention of human resources, interagency cooperation, enactment of necessary legislation, TB control policies enabling rational implementation of the programme and facilitation of the procurement of quality-assured second-line drugs. In addition, the national TB control programme must be strengthened to prevent the emergence of more MDR-TB cases.

### 2.2.2 A rational case-finding strategy including accurate, timely diagnosis through quality-assured culture and DST

Accurate, timely diagnosis is the backbone of a sound national TB control programme. Drug-resistant TB must be diagnosed correctly before it can be treated effectively. Case-finding strategies may vary depending on the epidemiological situation and local capacity. In some settings all TB patients are tested with culture and DST. However, in most settings only patients with an increased risk of drug-resistant TB are tested (strategies on which risk groups to test are discussed in Chapter 5).

Quality-assured culture and DST are indispensable. Non-viable cultures, culture contamination and unreliable DST results have major consequences for both individual patients and the national TB control programme as a whole. Internal quality control and external quality assurance should therefore be in place, including a link for proficiency testing with a recognized reference laboratory such as one of the WHO-recognized supranational TB reference laboratories.

### 2.2.3 Appropriate treatment strategies that use second-line drugs under proper case management conditions

An appropriate treatment strategy consists of a rational method for designing the optimal treatment regimen, a patient-centred approach for delivering this regimen with direct observation, and a plan for monitoring and managing adverse drug reactions. Designing an optimal regimen requires professional expertise to consider several factors together, including:

- representative data on drug resistance surveillance (DRS) of well-defined local groups of TB patients, distinguishing new cases and different types of re-treatment cases;
- history of drug use in the country and in the individual;
- specific array of available second-line drugs;
- availability of DST to first- and selected second-line drugs;
- reliable options for delivering directly observed therapy (DOT) for up to two years.

A standardized regimen for certain groups of patients may be more appropriate than an individualized regimen in some countries, while in others the converse may be best.

The choice between hospitalization and ambulatory treatment depends on several factors in addition to the severity of the disease. Such factors include the availability of hospital beds with adequate infection control measures to prevent nosocomial transmission; the availability of trained personnel at hospitals and clinics to administer treatment and manage adverse drug reactions; the availability of a social support network to facilitate adherence to ambulatory treatment; and the presence of other clinical or social conditions in patients.

### 2.2.4 Uninterrupted supply of quality-assured antituberculosis drugs

Management of second-line drugs is complex, especially when individualized treatment regimens are used. Drugs are frequently changed as a result of adverse effects, delayed DST results and poor response to treatment. In addition, most second-line drugs have a short shelf-life, global production of quality-assured drugs is limited and drug registration may be a lengthy and costly process that is not always attractive to drug manufacturers. Steps to ensure uninterrupted drug supply must begin six months or more in advance of the anticipated need, and drug needs must be estimated as accurately as possible. Countries should use only drugs that are quality-assured by a stringent drug regulatory authority recognized by WHO. A list of prequalified second-line drugs and manufacturers is in preparation.

### 2.2.5 Standardized recording and reporting system

The specific characteristics of a DR-TB control programme include a recording system with differently defined categories for patient registration, culture and DST results, and monitoring of treatment delivery and response for 24 months. Cohort analysis includes interim indicators and treatment outcomes after two or more years, as well as treatment outcomes by treatment regimen and DST results. The set of case registration groups and treatment outcome definitions for MDR-TB used in these guidelines (Chapter 4) were developed through a process that involved the Stop TB Working Group on DOTS-Plus for MDR-TB (3). They can be used for conducting cohort analyses under the DOTS strategy. The redesigned recording and reporting system (see Chapter 18) is essential for evaluating programme performance and treatment effectiveness.

## 2.3 A plan for tailored integration of management of drug-resistant tuberculosis into national programmes

Management of drug-resistant TB should be fully integrated into the national TB control programme. The challenge involved in this integration should not be underestimated. However, the complexity of the process should not deter programmes from taking the necessary steps to allow all patients with drug-resistant TB access to life-saving treatment. If many of the drug-resistant cases are treated in the private sector, integration can be facilitated through PPM approaches. Box 2.1 depicts the three key steps of a plan for integrating the management of drug-resistant TB.

The most important consideration is the political will to deliver rational treatment to patients with drug-resistant TB as part of a sound national TB control programme. Following confirmation of political will, a needs assessment should be carried out. Box 2.2 lists the most relevant variables to consider.

**BOX 2.1**

**Key steps for integrating management of drug-resistant TB into national TB control programmes**

1. Assessment of political will to deliver rational treatment to patients with drug-resistant TB.
2. Needs assessment for drug-resistant TB control activities.
3. Design and implementation of a plan for management of drug-resistant TB and its stepwise integration into the national TB control programme.

**BOX 2.2**

**List of variables to consider when assessing needs for integrating management of drug-resistant TB into national TB control programmes**

- Magnitude and distribution of drug-resistant TB
- Prevailing drug-resistance patterns
- Options for case-finding
- Existing infrastructure of the health-care system
- Available laboratory capacity
- Resources available for DOT over a prolonged period
- Availability of financial resources
- Quality standards of the laboratory network
- Availability of human resources
- Training needs
- Existing legal framework for drug management of second-line drugs
- Needs for external technical assistance

The needs assessment will facilitate the design and implementation of a plan to meet the gaps identified, in terms of both infrastructure and functioning of the health-care system. Once the infrastructure is in place and the key functions such as a quality-assured TB laboratory are operating, a stepwise integration of activities to control drug-resistant TB can proceed within the national TB control programme. Stepwise integration means that those districts or administrative areas where the integration is more likely to succeed should be prioritized.

The design and implementation of a DR-TB control programme may vary between and within countries, depending on the local needs and resources available. Despite a wide range of acceptable strategies, essential requirements such as quality-assured laboratories for diagnosis and monitoring of treatment response, delivery of DOT and use of quality-assured second-line drugs should be met under all conditions to ensure proper case management and prevent the emergence of resistance to second-line drugs.

## 2.4 Summary

The framework approach to management of drug-resistant TB, summarized in Box 2.3, includes five essential components that form the basis for every national TB control programme that includes detection and treatment of drug-resistant TB.

### BOX 2.3 FIVE COMPONENTS OF THE DOTS STRATEGY AS APPLIED TO DRUG-RESISTANT TB

#### 1. Sustained political commitment

- Addressing the factors leading to the emergence of MDR-TB
- Long-term investment of staff and resources
- Coordination of efforts between communities, local governments and international agencies
- A well-functioning DOTS programme

#### 2. Appropriate case-finding strategy including quality-assured culture and drug susceptibility testing (DST)

- Rational triage of patients into DST and the DR-TB control programme
- Relationship with supranational TB reference laboratory

#### 3. Appropriate treatment strategies that use second-line drugs under proper case management conditions

- Rational treatment design (evidence-based)
- DOT
- Monitoring and management of adverse effects
- Properly trained human resources

#### 4. Uninterrupted supply of quality-assured second-line antituberculosis drugs

#### 5. Recording and reporting system designed for DR-TB control programmes that enables performance monitoring and evaluation of treatment outcomes

## References

1. *Treatment of tuberculosis: guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).
2. *An expanded DOTS framework for effective tuberculosis control*. Geneva, World Health Organization, 2002 (WHO/CDS/TB/2002.297).
3. Laserson KF et al. Speaking the same language: treatment outcome definitions for multidrug-resistant tuberculosis. *International Journal of Tuberculosis and Lung Disease*, 2005, 9(6):640–645.