

CHAPTER 5

Case-finding strategies

5.1 Chapter objectives

This chapter describes strategies for case-finding and diagnosis of patients with either suspected or confirmed drug-resistant TB. Several approaches to case-finding and enrolment into DR-TB control programmes are discussed, taking into consideration that such programmes may have limited technical and financial capacity. The strategies range from testing all patients with TB to testing only a selected group of patients.

5.2 General considerations

Programme strategies strive to identify patients and initiate adequate treatment for drug-resistant cases in a timely manner. Timely identification and prompt initiation of treatment prevent the patient from spreading the disease to others, acquiring further resistance and progressing to a state of permanent lung damage.

It is strongly recommended that programmes have representative DRS data for new patients, the different categories of re-treatment patients (failure after Category I, failure after re-treatment, default and relapse) and other high-risk groups. Without this information, or when it is only partially available, designing an effective case-finding strategy is difficult and may be impossible. DRS data for the different groups also enable the number of patients who should enter the programme to be calculated, which in turn greatly facilitates programme planning and drug procurement.

5.3 Targeting risk groups for drug susceptibility testing

These guidelines assume a general understanding of case-finding and diagnosis of active TB. This information can be reviewed in reference books on TB, including WHO publications (1–2).

Routine DST at the start of treatment may be indicated in patients (or groups of patients, i.e. failures of Category II treatment as listed above) at high risk for drug resistance. These groups should be identified by representative DRS.

Specific elements of the history that suggest an increased risk for drug resistance are listed in Table 5.1. Stronger risk factors are placed higher in the

table. However, the prevalence of resistance in specific risk groups can vary greatly across different settings. The routine use of DST and the inclusion in Category IV treatment of patients with these risk factors is therefore not recommended for all groups listed. Instead, programmes should examine DRS data in risk groups together with their technical capacity and resources to determine which groups of patients should get routine DST.

5.4 Strategies for programmes with minimal access to DST and limited resources

Access to DST is required in all programmes. Under exceptional circumstances, and while building the laboratory capacity to perform DST, programmes may use strategies to enrol patients with a very high risk of MDR-TB in Category IV regimens without individual DST. For example, the results of representative DRS surveys may identify a group or groups of patients with a very high percentage of MDR-TB (percentages in these groups can often exceed 80%), which can justify the use of Category IV regimens in all patients in the group.

The three groups that are most likely to be considered for direct enrolment in Category IV regimens are discussed below.

- **Category II failures (chronic TB cases)** (3–4). Patients in whom Category II treatment failed in sound national TB control programmes often have MDR-TB (1–2). If the quality of DOT is poor or unknown (i.e. if regular ingestions of the medicines during Category II treatment are uncertain), patients may fail Category II treatment for reasons other than MDR-TB.
- **Close contacts of MDR-TB cases.** Category IV regimens for patients who are close contacts of MDR-TB cases are recommended in many, but not all, circumstances (see Chapter 14).
- **Category I failures.** Since the prevalence of MDR-TB in this group of patients may vary greatly, the rate in this group must be documented before deciding whether enrolment in DR-TB control programmes can take place without DST. Programmes should conduct DRS surveys to confirm that the routine use of Category II regimens is justified for patients in whom Category I treatment failed.

The percentage of MDR-TB in these three groups can vary. These guidelines strongly recommend confirming treatment failure by culture and testing for MDR-TB through the use of DST to at least isoniazid and rifampicin for all patients who start a Category IV regimen following this strategy. All programmes should therefore have capacity for DST.

TABLE 5.1 **Target groups for drug susceptibility testing**

RISK FACTORS FOR DRUG-RESISTANT TB	COMMENTS
Failure of re-treatment regimens and chronic TB cases	Chronic TB cases are defined as patients who are still sputum smear-positive at the end of a re-treatment regimen. These patients have perhaps the highest MDR-TB rates of any group, often exceeding 80% (1-2).
Exposure to a known MDR-TB case	Most studies have shown close contacts of MDR-TB patients to have very high rates of MDR-TB. Management of MDR-TB contacts is described in Chapter 14.
Failure of Category I	Failures of Category I are patients who while on treatment are sputum smear-positive at month 5 or later during the course of treatment. Not all patients who fail a regimen have MDR-TB, and the percentage may depend on a number of factors, including whether rifampicin was used in the continuation phase and whether DOT was used throughout treatment. More information on regimen implications for Category I failures is given below in this chapter and in Chapter 7.
Failure of antituberculosis treatment in the private sector	Antituberculosis regimens from the private sector can vary greatly. A detailed history of drugs used is essential. If both isoniazid and rifampicin were used, the chances of MDR-TB may be high. Sometimes second-line antituberculosis drugs may have been used, and this is important information for designing the re-treatment regimen.
Patients who remain sputum smear-positive at month 2 or 3 of SCC	Many programmes may choose to do culture and DST on patients who remain sputum smear-positive at months 2 and 3. This group of patients is at risk for MDR-TB, but rates can vary considerably.
Relapse and return after default without recent treatment failure	Evidence suggests that most relapse and return after default cases do not have MDR-TB. However, certain histories may point more strongly to possible MDR-TB; for example, erratic drug use or early relapses.
Exposure in institutions that have MDR-TB outbreaks or a high MDR-TB prevalence	Patients who frequently stay in homeless shelters, prisoners in many countries and health-care workers in clinics, laboratories and hospitals can have high rates of MDR-TB.
Residence in areas with high MDR-TB prevalence	MDR-TB rates in new cases in many areas of the world can be high enough to justify routine MDR-TB testing in all new cases.
History of using antituberculosis drugs of poor or unknown quality	The percentage of MDR-TB caused by use of poor-quality drugs is unknown but considered significant. It is known that poor-quality drugs are prevalent in all countries. All drugs should comply with quality-assured WHO standards.

TABLE 5.1 Target groups for drug susceptibility testing (*continued*)

RISK FACTORS FOR DRUG-RESISTANT TB	COMMENTS
Treatment in programmes that operate poorly (especially recent and/or frequent drug stock-outs)	These are usually non-DOTS or DOTS programmes with poor drug management and distribution systems.
Co-morbid conditions associated with malabsorption or rapid-transit diarrhoea	Malabsorption may result in selective low serum drug levels and may occur in either HIV-negative or -positive patients.
HIV in some settings	The 1999–2002 Global Surveillance did not find HIV to be a risk factor. However, numerous MDR-TB outbreaks have been documented in HIV patients, and in some areas of the world HIV is a risk factor for MDR-TB (see Chapter 10).

SCC = short-course chemotherapy

5.5 Information on DST specimen collection

If DST is chosen as part of the case-finding strategy, it is recommended that at least two, and preferably three, sputum specimens be obtained for culture and that DST be performed with the specimen that produces the best culture. DST does not routinely need to be carried out in duplicate. Procedures for collecting and managing specimens for culture and DST are described in Chapter 6, which also addresses different techniques, limitations, quality assurance requirements and other issues of culture and DST.

Previously treated patients may have had DST in the past but it may no longer reflect the resistance pattern of the strain they have at the time of enrolment in the DR-TB control programme. Programmes that base treatment on DST (individualized treatment) should repeat DST in all patients who have received treatment since the collection of their previous DST specimen.

Paediatric cases require adjustments in diagnostic criteria and treatment. Younger children in particular may not be able to produce sputum specimens on demand. Measures such as nasal gastric aspiration may be considered if this service is available. Programmes should not exclude children from treatment solely because sputum specimens are not available; smear- and culture-negative children with active TB who are close contacts of patients with MDR-TB can be started on Category IV regimens (see Chapter 14).

5.6 Case-finding of patients with mono- and poly-drug resistance

Mono- and poly-drug resistant strains are strains that are resistant to anti-tuberculosis drugs but not to both isoniazid and rifampicin. Most diagnostic strategies used by DR-TB control programmes will also identify cases of

BOX 5.1 COUNTRY EXAMPLES OF CASE-FINDING STRATEGIES

Example 1. Country A has an MDR-TB prevalence of 8% in cases newly diagnosed with the disease without history of previous antituberculosis treatment. The country has quality-assured DST laboratories for the first-line antituberculosis drugs. The national TB control programme has decided their programme has the capacity and resources to do DST of the following drugs in all patients: H, R, E and S. Patients identified with resistance will enter Category IV (options on how to design Category IV regimens and whether to do further DST testing are discussed in Chapters 7 and 8).

Example 2. Country B has an MDR-TB incidence of 3% in cases newly diagnosed with the disease, and there has been minimal use of second-line drugs for the treatment of TB. The country has a very high incidence of TB, exceeding 350 new cases per 100 000 people per year. It has access to quality-controlled DST laboratories for first-line drugs but not the capacity or resources to conduct DST for every TB case. The national TB control programme has decided to test all failures, relapses and returns after default for resistance to HRES. Different Category IV regimens are designed for different resistance patterns found (options on how to design these different Category IV regimens and whether to do further DST testing are discussed in Chapters 7 and 8).

Example 3. Country C has made minimal use of second-line drugs for the treatment of TB. There is currently no local laboratory to do DST. A thorough survey has shown that failures of Category I with 4HRZE/6HE (for notation on the standard code on how to write regimens with abbreviations see Chapter 7, section 7.6) have an MDR-TB prevalence of 11%. Return after default and relapse cases have MDR-TB rates below 4%. In the survey, failures of Category II (chronic cases) have an MDR-TB rate of 78%. Patients with MDR-TB are almost all susceptible to Km, Cm, Eto, Cs and PAS (exceeding 95% for each drug).

The survey in Country C was done with a precision of $\pm 4\%$. It is decided that all failures of Category I, relapses and returns after default will enter Category II regimens. Patients who do not respond well to Category II treatment and all failures of Category II will be entered into standardized Category IV regimens without testing for DST (options on how to design the Category IV regimens are described in Chapter 7). Ongoing surveillance data from an external laboratory will be used to evaluate whether the above protocol is adequate for failures of Category I and Category II, relapses and returns after default. Local DST will be built in the country in the coming years and the protocol re-evaluated once it is established.

Example 4. Country D has fairly good access to DST and resources to do testing. Rates of MDR-TB in cases newly diagnosed with the disease without history of previous antituberculosis treatment are low at 1.2%. Country D chooses to do DST on any patient who remains sputum smear-positive after month 2 of SCC. When DST results return, regimens are adjusted if resistance is found.

mono- and poly-drug resistance, in addition to MDR-TB cases. Patients with mono- or poly-drug resistance may require modifications to their short-course chemotherapy regimens or to be moved to Category IV (see Chapter 8).

5.7 Use of second-line DST in case-finding

Not all DR-TB control programmes have the capacity to do DST of second-line drugs. Furthermore, the clinical relevance of second-line DST is not well known (see Chapter 6). Many programmes therefore design diagnostic and treatment strategies that are not dependent on second-line DST. Commonly, programmes will carry out DST of second-line drugs on strains after their identification as MDR-TB. However, some programmes will carry out DST of second-line drugs at the initial evaluation if the suspicion of MDR-TB is very high and if most cases of MDR-TB in the area have shown high rates of resistance to second-line drugs. DST of second-line drugs and the interpretation of the results are discussed in Chapters 6 and 7.

References

1. *Treatment of tuberculosis: guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).
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4. Saravia JC et al. Re-treatment management strategies when first-line tuberculosis therapy fails. *International Journal of Tuberculosis and Lung Disease*, 2005, 9(4):421–429.