Executive summary

Multidrug-resistant tuberculosis (MDR-TB), defined as TB caused by organisms that are resistant to isoniazid and rifampicin, two first-line anti-TB drugs, continues to threaten the progress made in controlling the disease. The emergence of extensively drug-resistant TB (XDR-TB), defined as MDR-TB that is resistant as well to any one of the fluoroquinolones and to at least one of three injectable second-line drugs (amikacin, capreomycin or kanamycin), has heightened this threat. XDR-TB has been identified in all regions of the world since 2006. Treatment outcomes are significantly worse in XDR-TB patients than in MDR-TB patients. Outbreaks of XDR-TB in populations with high prevalence of HIV have caused alarmingly high mortality rates. The emergence of XDR-TB as a new threat to global public health demands that health officials and health-care providers respond with a coordinated strategy drawing on the Stop TB Strategy.[1]

Guidelines for the programmatic management of drug-resistant tuberculosis: emergency update 2008 provides updated guidelines and recommendations on how to manage drug-resistant TB (DR-TB) based on a rapid assessment of the best available evidence by a group of experts. A fully revised second edition will be published in 2010, following WHO guidance on retrieval, synthesis and grading of evidence. Until that time, the emergency update serves as interim guidance for TB control programmes and medical practitioners on all aspects of the management of DR-TB, including XDR-TB. It contains 19 chapters based on the original 18 chapters from the first edition published by the World Health Organization in 2006[2] plus an additional chapter on patient-centered care.

[1] The Stop TB Strategy launched by the World Health Organization in 2006 describes the recommended interventions that should be implemented to achieve the targets for global TB control that have been established within the context of the Millennium Development Goals. See Raviglione MC, Uplekar MW. WHO's new Stop TB Strategy. *Lancet*, 2006, 367:952–955.

[2] *Guidelines for the programmatic management of drug-resistant tuberculosis*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.361).

The key changes for the emergency update 2008 are summarized below.

CHAPTER	KEY RECOMMENDATIONS (* indicates updated recommendation)	KEY CHANGES
Chapter 1 Background information on drug-resistant tuberculosis	Not applicable	• Target audience is defined. • Development of guidelines is described. • Stop TB Strategy is summarized. • New data are provided from the WHO/IUATLD Global Project on Antituberculosis Drug Resistance Surveillance. • Updated information is provided from a survey of the network of supranational reference laboratories to determine the prevalence of XDR-TB among strains sent for drug susceptibility testing (DST).
Chapter 4 Definitions: case registration, bacteriology and treatment outcomes	Not applicable	• Definition of XDR-TB is introduced. • Concise instructions for registration of new cases of XDR-TB are provided.
Chapter 5 Case-finding strategies	• All patients at increased risk for MDR-TB should be screened for drug resistance.* • Patients infected with HIV should receive DST at the start of anti-TB therapy to avoid mortality caused by unrecognized MDR-TB.* • Rapid DST should be used for the initial screening of MDR-TB whenever possible. • Patients at increased risk for XDR-TB should receive DST of isoniazid, rifampicin, second-line injectable agents and a fluoroquinolone.*	• Stronger emphasis is placed on the recommendation that all patients at increased risk for MDR-TB should receive DST, with the goal of universal access to DST for all that need it. • The use of rapid DST in all HIV-infected patients who are smear-positive is highly encouraged, and it is recommended that all HIV-infected patients at moderate to high risk be screened for resistance in order to avoid the high mortality associated with unrecognized MDR-TB. • An algorithm for the use of rapid drug-resistance testing is introduced. • The use of DST for second-line drugs in case-finding for XDR-TB is introduced, and risk factors for XDR-TB are described.

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Chapter 6 Laboratory aspects	• All patients with suspected MDR-TB or XDR-TB need access to laboratory services for adequate and timely diagnosis. • Laboratories should be tested for proficiency and quality assured externally to perform DST.* • Laboratories should perform DST for the fluoroquinolones and second-line injectable agents where adequate capacity and expertise exists.* • DR-TB strains can be transported safely across international borders if international procedures and guidelines are followed.* • Laboratories must follow all standardized protocols for infection control and biosafety. • Quality control and quality assurance should be in place for microscopy, culture and DST. Links with supranational reference laboratories are strongly encouraged.	• Definitions of common terms used in laboratory issues are provided at the start of the chapter. • New recommendations for DST to second-line drugs are proposed based on recent WHO policy guidance; • References for regulations on how to transport infectious specimens internationally are provided.
Chapter 7 Treatment strategies for MDR-TB	• Design regimens with a consistent approach based on the hierarchy of the five groups of anti-TB drugs. • Promptly diagnose MDR-TB and initiate appropriate therapy. • Use at least four drugs with either certain, or almost certain, effectiveness. • DST should generally be used to guide therapy; however, do not depend on DST of ethambutol or pyrazinamide in individual regimen design, pyrazinamide, Group 4 and 5 drugs. • Do not use ciprofloxacin as an anti-TB agent in management of DR-TB.** • Design a programme strategy that takes into consideration access to quality-assured DST, rates of DR-TB, HIV prevalence, technical capacity and financial resources.	• The five groups of anti-TB drugs are re-defined. Thioacetazone is placed in Group 5. High-dose isoniazid and imipenem are added to Group 5. • Ciprofloxacin is removed as an anti-TB agent because of its weak efficacy compared with other fluoroquinolones. • Strong caution is warranted for any programme that uses gatifloxacin given the rare but dangerous adverse effects of dysglycaemia associated with this drug. • A new review of DST of second-line drugs has resulted in strong caution against basing the design of individual regimens on results of DST of ethambutol, pyrazinamide, or Group 4 and 5 drugs.

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Chapter 7 (*continued*)	• Treat MDR-TB patients for 18 months past the date of culture conversion. • Use adjunct therapies including surgery and nutritional or social support. • Treat XDR-TB aggressively whenever possible. • Treat adverse effects immediately and adequately.	• Table 7.2 is new and summarizes programme strategies accepted by the Green Light Committee that take into consideration quality of DST, rates of DR-TB, technical capacity and financial resources. • The management of XDR-TB is introduced.
Chapter 10 HIV infection and MDR-TB	• Perform provider-initiated HIV testing and counselling in all TB suspects.* • Use standard algorithms to diagnose pulmonary and extra-pulmonary TB. • Use mycobacterial cultures and, where available, newer more rapid methods of diagnosis. • Determine the extent (or prevalence) of anti-TB drug resistance in patients with HIV. • Introduce antiretroviral therapy (ART) promptly in MDR-TB or XDR-TB /HIV patients. • Consider empirical therapy with second-line anti-TB drugs.* • Provide co-trimoxazole preventive therapy (CPT) as part of a comprehensive package of HIV care to patients with active TB and HIV.* • Arrange treatment follow-up by a specialized team. • Implement additional nutritional and socioeconomic support. • Ensure effective infection control. • Involve key stakeholders in MDR-TB/HIV activities. • Monitor overlying toxicity with ART and DR-TB therapy.	• Stronger emphasis is placed on performing DST of HIV-infected individuals at the start of anti-TB therapy in areas of moderate or high MDR-TB prevalence. This subject is also introduced in Chapter 5 as a key change. • Greater detail is provided on the concomitant treatment of HIV and MDR-TB, including discussion of immune reconstitution inflammatory syndrome. • Table 10.3 provides a list of potential overlapping and additive toxicities of ART and anti-TB therapy.

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Chapter 11 Initial evaluation, monitoring of treatment and management of adverse effects	• Standard monitoring should be implemented for all patients on MDR-TB treatment. • Results both of sputum smear and culture should be monitored monthly to evaluate treatment response.* • Increased monitoring is required in HIV cases and for patients on ART.* • Health-care workers in MDR-TB control programmes should be familiar with the management of common adverse effects of MDR-TB therapy. • Ancillary drugs for the management of adverse effects should be available to the patient.	• New recommendations for monitoring the response to treatment are described. • Laboratory monitoring for patients receiving both ART and MDR-TB therapy is added to Table 11.1.
Chapter 12 Treatment delivery and adherence	• Use disease education, DOT, socioeconomic support, emotional support, management of adverse effects and monitoring systems to improve adherence to treatment. • National TB control programmes (NTPs) are encouraged to incorporate community-based care and support into their national plans.*	• A section on community-based care and support is added to this chapter. NTPs are encouraged to add community-based care and support into their national strategies and plans.
Chapter 14 Management of contacts of MDR-TB patients	• MDR-TB contact investigation should be given high priority, and NTPs should consider contact investigation of XDR-TB as an emergency situation.*	• NTPs should consider contact investigation of XDR-TB as an emergency situation.
Chapter 15 Drug resistance and infection control	• Infection control, including administrative and engineering controls as well as personal protection, should be made a high priority in all MDR-TB control programmes. • XDR-TB patients should be placed isolated following a patient-centred approach and WHO ethical and legal guidance until no longer infectious.*	• Infection control measures are proposed, with special attention to XDR-TB and the high mortality of patients coinfected with HIV and DR-TB. • XDR-TB patients should be placed in ward isolation until no longer infectious. • MDR-TB patients should receive routine care outside of normal HIV care settings.

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Chapter 18 Category IV recording and reporting system	• A standardized method of recording and reporting should be implemented in DR-TB control programmes. • DR-TB treatment cards should have an expanded section for information on patients with HIV.* • The International Health Regulations (IHR2005) should be followed.*	• Chapter 18 has been rewritten to be simpler and more consistent with the DOTS recording and reporting system. • The treatment card described in Chapter 18 has an expanded section for information on patients with HIV. • Box 18.1 provides additional recording and reporting components, which are optional for programmes. • The International Health Regulations 2005 should be followed.
Chapter 19 Managing DR-TB through patient-centered care	Not applicable	• Chapter 19 is the only completely new chapter in this revision. Any patient in whom MDR-TB or XDR-TB is suspected or diagnosed should be provided with high-quality patient-centered care, as outlined in both the International Standards for Tuberculosis Care, the Patients' Charter for Tuberculosis Care and in the WHO Good Practice in Legislation and Regulations for TB Control.