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Tuberculosis Handbook

Second edition

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Contents

Preface

Since the publication of the *Tuberculosis handbook* by the World Health Organization in 1998, important changes have taken place in the global context in which control of tuberculosis (TB) is carried out. Firstly, the DOTS strategy has been adopted by virtually all countries during the past decade, although with varying quality, and full-scale DOTS implementation has not yet been achieved. At the same time, efforts to control the disease have become increasingly patient-centred and directed towards universal access to care for all.

Secondly, new major challenges to public health have emerged, adding complexities for the work of national TB control programmes (NTPs) and straining available resources. The epidemic of infection with the human immunodeficiency virus (HIV) has become the main driving force behind the increasing incidence of TB in sub-Saharan Africa and elsewhere, requiring NTPs to reach beyond their usual mandate and to work jointly with HIV control services; they have also had to face the emergence of multidrug-resistant TB (MDR-TB) and, most recently, extensively drug-resistant TB (XDR-TB) in many countries. Addressing drug-resistant TB requires a massive increase of resources both to treat patients with second-line drugs and to prevent the development of resistance, through general improvements in programme performance.

Thirdly, building health systems and primary services that provide access to health care for all brings new challenges. NTP managers should become engaged in and contribute to general system development, while expecting from systems and services the

contributions needed for TB control. Opportunities should therefore be sought to improve control of the disease while also contributing to the development of general health services.

Fourthly, the increasing involvement of the non-state sector in the care of TB patients, although welcomed, brings an additional challenge: ensuring that adequate standards of care (such as those contained in the *International standards for tuberculosis care*) are applied by all providers.

Fifthly, civil society and communities themselves are key elements in the fight against TB, but their engagement and empowerment need to be further promoted and facilitated. The recently published *Patients' charter for tuberculosis care*, based on input from affected communities worldwide, has not yet been widely adopted by NTPs. Social mobilization is an important innovative component of the Stop TB Strategy.

Finally, research on TB, neglected for decades, should be fostered to meet the increasingly pressing need for new drugs, diagnostics and vaccines. Addressing TB/HIV and MDR-TB requires improved and rapid diagnostic tools; new classes of drugs are needed for MDR-TB and XDR-TB, and to shorten the length of treatment; engaging non-state practitioners and communities requires operational research to fine-tune interventions. Eliminating TB requires effective preventive measures as well as optimal case management.

Taking account of these new and changing situations, the Stop TB Strategy defines specific objectives and components directed towards the overall target of Millennium Development Goal 6: to have halted and begun to reverse the incidence of TB by 2015. This new version of the *Handbook for national TB control programmes* provides an overview of the broad range of approaches needed to implement all six components of the Strategy, and to achieve its goals. It is the result of efforts by many experts, building on the new knowledge and evidence that are behind the complexities of modern TB control; its purpose is to facilitate the work of all those who are engaged in the aim of ultimately eliminating TB.

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Abbreviations

ACSM	advocacy, communication and social mobilization
AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
BCG	bacille Calmette–Guérin (vaccine)
BMU	basic management unit
BSC	biosafety cabinet
BSL	biosafety level
CBO	community-based organization
CPT	co-trimoxazole preventive therapy
CXR	chest X-ray (examination)
DOT	directly observed therapy
DRS	drug resistance surveillance
DST	drug susceptibility testing
EQA	external quality assurance
FBO	faith-based organization
FDC	fixed-dose combination (anti-TB medicines)
GDF	Global Drug Facility
GDP	good distribution practice
GLC	Green Light Committee
GMP	good manufacturing practice
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria

HEPA	high efficiency particulate air
HIV	human immunodeficiency virus
HRD	human resource development
HRH	human resources for health
HSS	health system strengthening
IEC	information, education and communication
IHR	International Health Regulations
IMAI	integrated management of adult and adolescent illness
IMCI	integrated management of childhood illness
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
KAP	knowledge, attitudes and practices
LTBI	latent TB infection
MCH	maternal and child health
MDG	Millennium Development Goal
MDR-TB	multidrug-resistant tuberculosis
MTEF	medium-term expenditure framework
MTSP	medium-term strategic plan
NGO	nongovernmental organization
NRL	national reference laboratory
NTP	national tuberculosis control programme
PAL	practical approach to lung health
PHC	primary health care

PLHIV	people living with HIV
PPM	public–private mix
PRSP	poverty reduction strategy paper
PT	preventive therapy
PTB	pulmonary tuberculosis
QC	quality control
SCC	short-course chemotherapy
SWAP	sector-wide approach
TB	tuberculosis
TST	tuberculin skin test
Union	International Union Against Tuberculosis and Lung Disease
UNICEF	United Nations Children's Fund
UVGI	ultraviolet germicidal irradiation
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis

Introduction

An adequate strategy for the control of tuberculosis (TB) globally calls for a comprehensive approach to address all the main constraints to control of the disease, including emerging challenges, as well as the main factors influencing the incidence of TB, such as socioeconomic and environmental aspects. Consequently, the scope of activities undertaken by national TB control programmes (NTPs) has greatly increased. The purpose of this handbook is to bring together in summarized form the issues, recommended strategies and practical measures involved in addressing each of the components of the Stop TB Strategy. It outlines the range of activities to be addressed by NTPs and the recommended approaches to implementation of the Strategy.

This publication draws upon current guidelines and information documents issued by the World Health Organization (WHO), which provide more detailed guidance on implementation for each of the specific subject areas. The listed references are limited to key readings for implementation of programme activities and to texts that provide important additional background and supplementary information. As further information becomes available, it will be provided on the WHO web site.[1] Readers are advised to consult this web site periodically for updated information and guidance.

The structure and organization of the handbook follow and reflect the components of the Stop TB Strategy. Parts I and II are concerned mainly with components 1 and 2 of the

[1] www.who.int/tb/en

strategy; Part III covers its new elements, i.e. components 3, 4, 5 and 6. However, because the strategy is integrated within the activities of NTPs, many issues are cross-cutting and relevant across all parts of this publication.

This handbook was prepared principally for use by NTP managers and staff, as well as partner organizations and all professionals involved in delivering TB care and implementing TB control activities. Readers are provided with a concise account of the essential elements of a comprehensive TB control programme and an overview of the full range of activities that need to be implemented to achieve the TB control targets set for 2015. The focus is on the recommended approaches and measures to be taken, in accordance with the referenced guidelines and other documents that provide more detailed information on implementation.

Implementing the Stop TB Strategy: a handbook for national TB control programmes is the successor to the *Tuberculosis handbook* published by WHO in 1998. The contents of the printed book are expected to remain valid for at least five years from the date of publication, with updated information provided on specific issues on the WHO web site as it becomes available. The printed edition will be considered for possible revision after 2010.

Methodology

This publication is an abridged version of the guidance and information detailed in a series of recently produced WHO guidelines, publications on systematic reviews and information documents. These documents are themselves based upon best available evidence, including

clinical trials in some instances, as well as the accumulated experience from NTPs worldwide, which reported some 90 million TB cases to WHO between 1980 and 2005. In rapidly changing subject areas where available information on the efficacy and effectiveness of the recommended measures is limited, guidance is based on expert opinion and best practices derived from experience gained in TB control and other health programmes, as of the publication date of this handbook.

The *International standards for tuberculosis care* describe a widely accepted level of care that all practitioners – public and private – should seek to achieve in managing patients who have, or are suspected of having, TB. They include a comprehensive list of the published original research and systematic reviews that inform the WHO recommendations contained in this handbook on the diagnosis and treatment of TB. Extensive reference lists are also provided in *Toman's tuberculosis: case detection, treatment, and monitoring*. Each chapter lists relevant WHO guidelines and key peer-reviewed texts on which the chapter is based.

A broad international consultative process was used to draft this document. The process involved the following five steps:

1. Establishment of a Stop TB Department steering group (12 people) responsible for planning the structure and organization of the handbook; selecting the members of the review group; providing guidance to a consultant who coordinated the development of the text; and considering the comments received from reviewers.

2. Appointment of a writing committee comprising staff from the Stop TB Department and the Stop TB Partnership Secretariat (24 people), including technical focal point staff members for each subject area, responsible for ensuring the accuracy of the technical content of specific sections and considering the comments of reviewers.

3. Establishment of an international expert review group (24 people) including representatives from a broad range of technical partner agencies as well as technical experts, NTP managers and staff from WHO headquarters and regional offices.

4. Review of the complete draft text by the international review group. All comments were considered by the technical focal point staff and followed up as appropriate, including further discussion with reviewers and consideration by the steering group as necessary. All comments received were kept on record. Most of the reviewers' comments were incorporated, with the exception of those that were either (i) inconsistent with current WHO policy or (ii) went beyond the scope of this publication.

5. Amendment of the text on the basis of the comments received from the international review group. Review of the amended text by the steering group and final revision.

6. Conflict of interest. All participants involved in the preparation and review of the text completed a Declaration of Interests. No conflict of interest was declared by any participant.

Epidemiology of tuberculosis

Tuberculosis remains a major cause of morbidity and mortality in many countries and a significant public health problem worldwide. The global incidence of TB was estimated to be 136 cases per 100 000 population per year in 2005, ranging from 39 per 100 000 per year in the WHO Region of the Americas to 343 per 100 000 per year in the WHO African Region. This represents a total of 8.8 million new cases of TB and 1.6 million deaths from TB every year. The 22 high-burden countries, as defined by WHO, are those countries that cover 63% of the world's population and that account for approximately 80% of the estimated number of new TB cases occurring worldwide each year; some of these countries are also among those with the highest incidence rates of TB per capita. WHO publishes an annual report on global tuberculosis control that details the latest surveillance and survey data.

Before the introduction of chemotherapy, WHO estimated that, on average, one infectious source would transmit infection by *Mycobacterium tuberculosis* to 20 others during an average of two years before death or self-cure. Thus, a population of 100 000 people with 50 new cases of smear-positive TB occurring every year would produce 100 infectious cases in the population at any given time, leading to 1000 new infections annually, i.e. 1% of the population becoming infected every year.

Of all those infected with *M. tuberculosis*, about 5% will develop active TB disease within five years of primary infection; the other 95% will develop a latent infection that may later progress to cause disease, depending on the status of the immune system. Overall, about 10% of infected individuals will eventually develop active TB.

In the absence of infection with human immunodeficiency virus (HIV) and without anti-TB treatment, about 65% of cases who remain smear-positive will die, most within two years, while only 10–15% of cases who remain smear-negative are expected to die. Even with treatment, more than 10% of patients may die in settings where adherence to treatment is low or where rates of HIV infection or drug resistance are high. In places where treatment is good and HIV is absent, fewer than 2% of smear-positive patients die while on treatment. The risk of developing TB increases with age after puberty, particularly among men, who have both a higher rate of infection and a higher risk of progression to active TB disease over the course of their lives than women. The risk of developing severe forms of disease in organs other than the lungs (e.g. tuberculous meningitis) is higher in children aged under 5 years than in older children and adults.

The most important recent changes in the natural history of TB have been the impact of the HIV epidemic and the emergence of resistance to anti-TB drugs.

HIV infection exacerbates the TB epidemic through its impact on susceptibility to *M. tuberculosis* infection and progression from infection to active disease. HIV infection increases the rate at which *M. tuberculosis* infections are acquired and increases the likelihood that people who are already infected will develop active TB disease. The impact of HIV has been greatest in countries of southern and eastern Africa, where up to 40% of adults may be infected with HIV and where the incidence of TB has increased 4–5-fold within 10 years. Infection with both *M. tuberculosis* and HIV is prevalent in some population groups in

certain countries of South-East Asia, including Cambodia, China, India, Thailand and Viet Nam. Other significant risk factors may also have an important impact at population level, depending on the degree of exposure to these risk factors in the population.

The development and increasing importance of anti-TB drug resistance are of concern to NTPs because drug-resistant TB is much more difficult and costly to treat than fully drug-susceptible TB. An estimated 450 000 cases of multidrug-resistant TB (MDR-TB) occur each year among new and previously treated TB cases, and extensively drug-resistant TB (XDR-TB) has been reported from many countries. Drug resistance emerges where cure rates are low, for example where anti-TB drugs are available without medical prescription. It is for this reason that NTPs have been advised over the years to concentrate on achieving high cure rates and optimizing the quality of and access to anti-TB drugs, on increasing case detection rates, on ensuring good treatment outcomes for patients with MDR or XDR-TB and, in settings where HIV is prevalent, on ensuring that TB patients are tested for HIV and that people with HIV are examined for TB.

Other factors may also have a significant effect on the distribution of TB in populations, and on TB trends over time. Factors that affect exposure to *M. tuberculosis* infection and progression to active TB include overcrowding, tobacco smoking, diabetes and malnutrition. Their influence on the TB epidemic depends on the level of risk per person and on their prevalence in the population, quantities that are as yet poorly defined.

Within the framework of the Millennium Development Goals (MDGs), the main target for TB control is to ensure that the global incidence rate falls by 2015. Supplementary targets, endorsed by the Stop TB Partnership, are to halve the 1990 prevalence and death rates by 2015. Observations on NTPs, backed by mathematical modelling, indicate that in the absence of HIV, the detection of 70% of infectious cases occurring each year and cure of at least 85% of them should reduce the incidence of TB at a rate of about 5–10% per year. If an annual rate of decline of 5% or more is achieved shortly, it should be possible to meet the MDG and Stop TB Partnership targets globally by 2015.

The Stop TB Strategy

Major progress in global TB control followed the widespread implementation of the DOTS strategy in countries with a high burden of TB. However, global statistics indicated that DOTS alone would not be sufficient to achieve global TB control and elimination. In 2005, the World Health Assembly recognized the need for a new strategy that would build upon and enhance the achievements of DOTS. The Stop TB Strategy, launched on World TB Day in 2006, is designed to meet the TB-related Millennium Development Goal (MDG) as well as the Stop TB Partnership targets set for 2015. The Stop TB Strategy underpins the *Global Plan to Stop TB 2006–2015*.

THE STOP TB STRATEGY AT A GLANCE

Vision	A world free of tuberculosis
Goal	• To reduce dramatically the global burden of tuberculosis (TB) by 2015 in line with the Millennium Development Goals (MDGs) and the Stop TB Partnership targets
Objectives	• To achieve universal access to high-quality diagnosis and patient-centred treatment • To reduce the suffering and socioeconomic burden associated with TB • To protect poor and vulnerable populations from TB, TB/HIV and multidrug-resistant TB (MDR-TB) • To support the development of new tools and enable their timely and effective use
Targets	• MDG 6, target 8 – to have halted and begun to reverse the incidence of TB by 2015 • Targets linked to the MDGs and endorsed by the Stop TB Partnership: — by 2005, to have detected at least 70% of new sputum smear-positive TB cases and cured at least 85% of these cases — by 2015, to have reduced TB prevalence and death rates by 50% relative to 1990 levels — by 2050, to have eliminated TB as a public health problem (<1 case per million population)

Components of the Strategy and implementation approaches

1. Pursuing high-quality DOTS expansion and enhancement
a. Political commitment with increased and sustained financing
b. Case detection through quality-assured bacteriology
c. Standardized treatment, with supervision and patient support
d. An effective drug supply and management system
e. Monitoring and evaluation system as well as impact measurement

2. Addressing TB/HIV, MDR-TB and other challenges
a. Implement collaborative TB/HIV activities
b. Prevent and control MDR-TB
c. Address prisoners, refugees and other high-risk groups, and special situations

3. Contributing to health system strengthening
a. Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery and information systems
b. Share innovations that strengthen systems, including the Practical Approach to Lung Health
c. Adapt innovations from other fields

4. Engaging all care providers
a. Public–public and public–private mix approaches
b. *International standards for tuberculosis care*

5. Empowering people with TB, and communities
a. Advocacy, communication and social mobilization
b. Community participation in TB care
c. *Patients' charter for tuberculosis care*

6. Enabling and promoting research
a. Programme-based operational research
b. Research to develop new drugs, diagnostics and vaccines

Source: *The Stop TB Strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.368).

Challenges to controlling TB

Control of TB globally continues to face major challenges. Efforts must continue to pursue high-quality DOTS expansion and enhancement. Addressing TB/HIV and MDR-TB requires increasing effort and resources, as do other challenges facing NTPs such as immigration and high-risk groups. Weak health systems and scarce human resources are constraints to programme implementation. Organizing standardized health services to provide a standardized approach to TB management within the public sector often excludes large numbers of patients, particularly the very poor, leaving them to the largely unregulated non-state sector. Access to high-quality care for TB patients is still limited by barriers of gender, age, type of disease, social setting and ability to pay the direct and indirect costs of care. Without the effective engagement of TB patients and communities, TB services may not reach those who need them most. Finally, without commitment to and wide support for research, including the development and deployment of new drugs, diagnostics and vaccines, the Stop TB Partnership goal of eliminating TB by 2050 is unlikely to be reached.

Innovative approaches and mechanisms

Complementary approaches to addressing the major challenges to TB control have been explored and promoted. New resources are increasingly available from national and international sources to support these initiatives, which include:

- collaborative activities between TB and HIV control programmes;
- strategies to manage drug-resistant TB;
- addressing TB control for marginalized and vulnerable population groups;

- improving access to quality-assured drugs for TB and drug-resistant TB through mechanisms such as the Global Drug Facility and the Green Light Committee respectively;
- initiatives that strengthen primary respiratory care in general while expanding high-quality TB services;
- options to address poverty in TB control;
- innovative strategies for engaging diverse public, voluntary, corporate and private providers to widen the network of TB services;
- adopting the *International standards for tuberculosis care* to ensure high quality of care across all care providers;
- empowering people through social mobilization and effective ways of undertaking community TB care;
- recognizing TB care as a basic human right, as set out in the *Patients' charter for tuberculosis care*;
- forging new alliances and initiatives for the development of new tools.

The Global Plan to Stop TB 2006–2015

The Global Plan reflects a consensus view of what the Stop TB Partnership can achieve by 2015, provided the resources are mobilized to implement the Stop TB Strategy according to the steps set out in the Global Plan. Over the 10-year plan period, it is projected that some 50 million people should be treated for TB through the Stop TB Strategy, including 1.5 million patients with MDR-TB, and about 3 million TB/HIV patients are expected to be enrolled on antiretroviral therapy (ART).

Importance of actions taken outside TB control programmes and outside the health sector

Control of TB should be seen as an integral part of country strategies to reduce poverty and advance development. Effective TB control requires addressing all risk factors that make individuals vulnerable to infection by *M. tuberculosis* and to developing disease. Actions taken by other health and development programmes are also required to reduce exposure to risk factors that increase vulnerability to TB infection and disease. TB control programmes should encourage and support such actions. Some of the drivers of the TB epidemic, including poverty, inequity, illiteracy and poor housing, need to be tackled mainly by actors outside the health sector. The role of programmes in this respect would be to identify the need for actions beyond these programmes and to effectively communicate this need and advocate for interventions to relevant decision-makers.

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Part I Tuberculosis care and prevention

This section reflects the patient-centred approach to TB control care, which is a fundamental principle of TB control as recommended by the Stop TB Strategy. It focuses on the care and management of patients and the reduction of risk for others. All aspects of case detection, diagnosis, treatment and case management of individual patients are included, as well as the available approaches to TB prevention. Specific issues concerning the diagnosis and treatment of drug-resistant TB and TB/HIV are emphasized in view of the increasing public health importance of these conditions. Chapter 4 is devoted to the management of TB in children, which requires special measures and different approaches to those for TB in adults.

Prevention of TB includes interventions to reduce transmission, and to reduce the risk of TB disease in infected persons. Some of the interventions result in specific activities of TB control programmes: contact tracing, detection of sources, infection control, preventive therapy, BCG vaccination, and treatment of HIV-infected persons with ARV. Other factors that strongly influence the risk of becoming exposed and infected (such as overcrowding) or developing active TB (such as HIV, poor nutrition, smoking, diabetes) often cannot be readily influenced by the TB control programme activities and resources and usually do not fall under the direct responsibility of the NTPs. However, the NTPs can play a strong advocacy role in attempting to alleviate the impact of these risk factors.

Chapter 1 Case detection

The detection of TB cases requires that affected individuals are aware of their symptoms, have access to health facilities and are evaluated by health workers (doctors, nurses, medical assistants, clinical officers) who recognize the symptoms of TB. Health workers must have access to a reliable laboratory and ensure that the necessary specimens are collected for examination. This is a complex set of activities and behaviours, and failure at any stage can cause delays in diagnosis or misdiagnoses.

The most common symptom of pulmonary TB is a persistent, productive cough, often accompanied by other nonspecific symptoms. Although the presence of a cough for 2–3 weeks is nonspecific, traditionally having a cough of this duration has served as the criterion for defining suspected TB and is used in most national and international guidelines.

The following symptoms of pulmonary TB may accompany cough and sputum production:

- *respiratory symptoms*: shortness of breath, chest and back pains, haemoptysis;
- *constitutional symptoms*: loss of appetite, weight loss, fever, night sweats, fatigue.

Symptoms of extrapulmonary TB are related to specific extrapulmonary sites, such as lymph nodes, pleura, larynx, meninges, genitourinary and intestinal tracts, bone, spinal cord, eye and skin.

Sputum smear microscopy. Sputum specimens should be obtained for microscopic examination from all patients suspected of having pulmonary TB. Microbiological diagnosis is confirmed by culturing *M. tuberculosis* (or, under appropriate circumstances, by identifying specific nucleic acid sequences in a clinical specimen) from any suspected site of disease. However, in many settings where resources are limited, neither culture nor rapid amplification methods are currently available or feasible. In such circumstances, the diagnosis of TB may also be confirmed by the presence of acid-fast bacilli (AFB) in sputum smear examination. Repeated sputum smear microscopy may diagnose pulmonary TB in up to two-thirds of active cases.

In nearly all clinical circumstances in settings of high TB prevalence, identification of AFB by microscopic examination is highly specific for the *M. tuberculosis* complex. Sputum smear microscopy is the most rapid method for determining whether a person has TB; it identifies people who are at greatest risk of dying from the disease and the most likely transmitters of infection.

Sputum specimens. The optimum number of sputum specimens to establish a diagnosis has been evaluated. The first specimen was found positive in 83–87% of all patients in whom AFB are ultimately detected; the second specimen was positive in an additional 10–12% and the third specimen in a further 3–5%. On this basis, WHO recommends the microscopic examination of two sputum specimens (formerly three).[1] Because the yield of AFB appears

[1] A reduction in the number of specimens examined for screening TB suspects from three to two was recommended by WHO and endorsed by the Strategic Technical and Advisory Group for Tuberculosis in June 2007.

to be greatest from early morning (overnight) specimens, WHO further recommends that at least one specimen should be obtained from an early morning collection.

Sputum collection procedures. The procedures for collecting sputum involve the production of droplets that are highly infectious if the patient has untreated pulmonary TB. Sputum collection should therefore be organized in areas with good ventilation or, if not available, outside the building (see Chapter 6).

Sputum smear specimens should be examined by microscopy immediately but no later than 5 to 7 days after they have been collected. A health unit without adequate facilities for collecting and transporting sputum should refer the patient to the nearest health unit able to collect sputum, or direct the patient to a microscopy laboratory.

National TB guidelines should include all the details of what health workers should do before, during and after the collection of sputum. Attention should be paid to the characteristics of sputum containers, precautions for health workers, labelling, identification and recording of patients' addresses.

Diagnosis of smear-negative tuberculosis. For smear-negative and extrapulmonary TB, a diagnosis by a clinician specially trained in TB may be required as well as radiographic examination. As no chest radiographic pattern is absolutely specific for pulmonary TB, the diagnosis of smear-negative TB is always presumptive and should be based on other clinical and epidemiological information, including failure to respond to a course of broad-spectrum

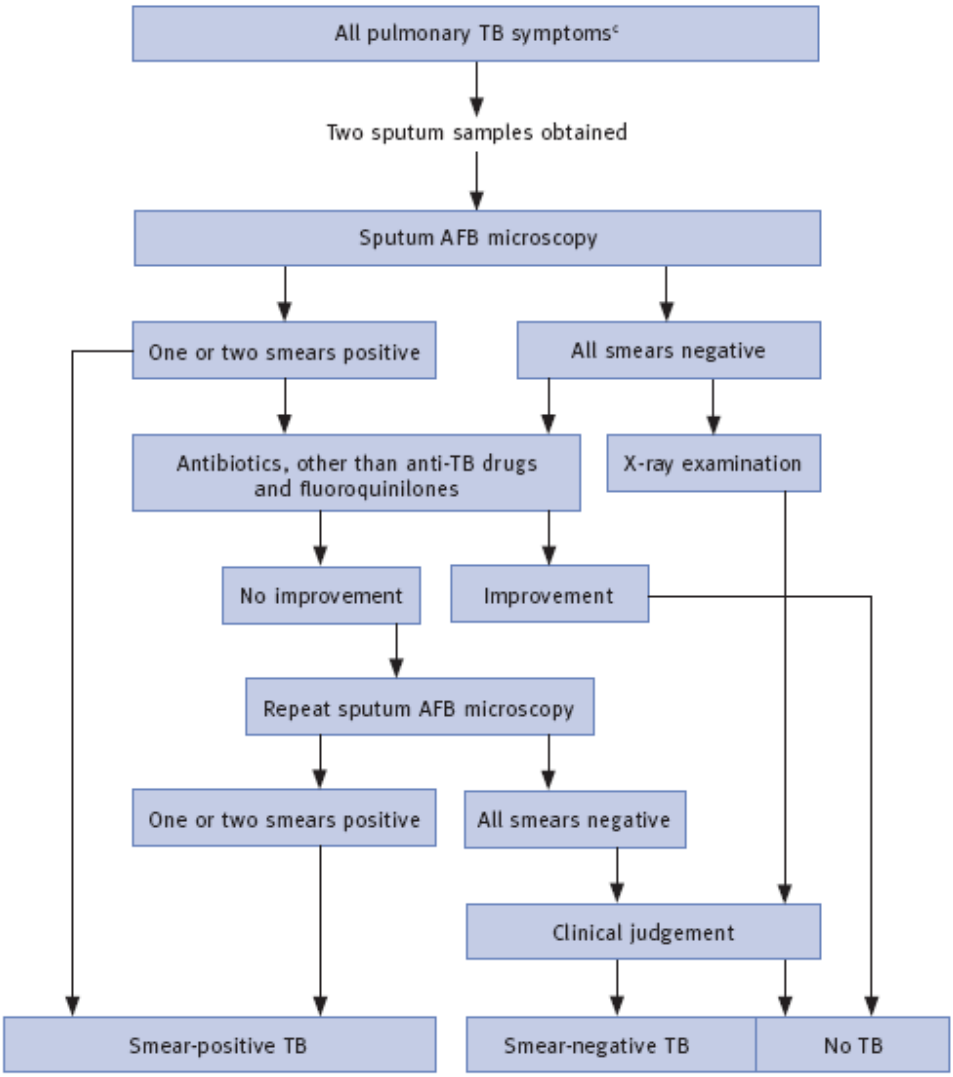
antibiotics and exclusion of other pathology. Reliance on chest radiography as the only diagnostic test for TB results in either overdiagnosis of TB or missed diagnoses of TB and other diseases and is therefore not recommended. Radiographic examination, however, is most useful when applied as part of a systematic approach to evaluate patients whose symptoms and/or findings suggest TB but whose sputum smears are negative. Fluoroscopy results are not acceptable as documented evidence of pulmonary TB.

Pregnancy. Case-detection methods in pregnancy should exclude radiographic examination, particularly in the first trimester.

Culture. While sputum smear microscopy is the first bacteriological diagnostic test of choice where adequate, quality-assured laboratory facilities are available, the evaluation of patients with negative sputum smears should also include culture. Culture adds extra cost and complexity but greatly increases the sensitivity and specificity of diagnosis, resulting in better case detection. Although the results of culture may not be available until after a decision to begin treatment has been made, treatment may be stopped subsequently if cultures from a reliable laboratory are negative, or if the patient has not responded clinically to treatment and the clinician has sought other evidence in pursuing the differential diagnosis.

Figure 1.1 presents an illustrative approach to the diagnosis of pulmonary TB in settings with a low prevalence of HIV infection. Diagnostic algorithms for high HIV-prevalent settings and for seriously ill patients are provided in section 1.3.

FIGURE 1.1 AN ILLUSTRATIVE APPROACH TO THE DIAGNOSIS OF SUSPECTED PULMONARY TUBERCULOSIS[a,b]



AFB = acid-fast bacilli; TB = tuberculosis

[a] Adapted from *Treatment of tuberculosis: guidelines for national programmes*. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

[b] Applicable for areas with low HIV prevalence.

[c] Screening: cough >2–3 weeks.

Extrapulmonary tuberculosis. Extrapulmonary TB (without associated lung involvement) accounts for 15–20% of TB in populations with a low prevalence of HIV infection. In populations with a high prevalence of HIV infection, the proportion of cases with extrapulmonary TB is higher. Because appropriate specimens may be difficult to obtain from some of these sites, bacteriological confirmation of extrapulmonary TB is often more difficult than for pulmonary TB. Relatively few *M. tuberculosis* organisms are present in extrapulmonary sites, and identification of AFB by microscopy in specimens from these sites is infrequent. For example, microscopic examination of pleural fluid in tuberculous pleuritis and tuberculous meningitis detects AFB in only about 5–10% of cases.

Given the low yield of microscopy, both culture and histopathological examination of tissue specimens, such as those that may be obtained by needle biopsy of lymph nodes, are important diagnostic tests for extrapulmonary TB.

1.1 Case definitions of tuberculosis

A diagnosis of TB should be followed by specification of the type of TB, i.e. the case definition, which is necessary for prescribing treatment according to standardized regimens, for patient registration and reporting, for cohort analysis of treatment outcomes and for determining trends.

Case definitions for TB take into account the anatomical site of disease, the bacteriological results, the severity of disease and the history of previous treatment. Tables 1.1 and 1.2

present the definitions of TB cases by site, bacteriological status and history of previous treatment in adult patients. The definition of a sputum smear-positive case is the same for HIV-positive and HIV-negative patients, i.e. requiring at least one positive smear in countries with a functional system of external quality assurance (EQA).

TABLE 1.1 CASE DEFINITIONS BY SITE AND BACTERIOLOGICAL STATUS IN HIV-NEGATIVE ADULTS AND FOR NON-HIV PREVALENT SETTINGS

Case classification	Definition
Pulmonary tuberculosis, sputum smear-positive (PTB+)	One or more initial sputum smear examinations positive for Acid-fast bacilli by microscopy
Pulmonary tuberculosis, sputum smear-negative (PTB–)	A case of pulmonary tuberculosis who does not meet the above definition for smear-positive tuberculosis. **Note:** In keeping with good clinical and public health practices, diagnostic criteria should include: 1. At least two sputum specimens negative for acid-fast bacilli, **and** 2. Radiographic abnormalities consistent with active pulmonary tuberculosis, **and** 3. No response to a course of broad-spectrum antibiotics, and 4. Decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy. This group includes patients whose sputum smears are negative but whose culture is positive.
Extrapulmonary tuberculosis	A patient with tuberculosis affecting organs other than the lungs. Diagnosis should be based on one culture-positive specimen, or histological or strong clinical evidence consistent with active extrapulmonary tuberculosis, followed by a decision by a clinician to treat with a full course of anti-tuberculosis chemotherapy.

TABLE 1.2 CATEGORY OF PATIENTS FOR REGISTRATION ON DIAGNOSIS (BASED ON HISTORY OF PREVIOUS TREATMENT)

Diagnostic/registration category		Definition
New		A patient who has never had treatment for tuberculosis or who has taken anti-tuberculosis drugs for less than one month.
Re-treatment cases	**Relapse**	A patient previously treated for tuberculosis who has been declared cured or treatment completed, and is diagnosed with bacteriologically positive (at least one smear or culture) tuberculosis.
	Treatment after failure	A patient who is started on a re-treatment regimen after previous treatment has failed.
	Treatment after default	A patient who returns to treatment with positive bacteriology, following interruption of treatment for two months or more.
Transfer in		A patient who has been transferred from another tuberculosis register to continue treatment in a different register area.
Other		All cases who do not fit the above definitions. This group includes patients who are sputum smear-positive at the end of a re-treatment regimen (previously defined as Chronic cases) and who may be resistant to the first-line drugs.

Note: Smear-negative pulmonary and extrapulmonary cases may also be relapses, failures or other cases. Such diagnoses should be supported by pathological or bacteriological evidence.

1.1.1 Anatomical site of disease

The two main categories of TB by anatomical site of disease are: (i) pulmonary TB, or disease affecting the lung parenchyma (the most common form of TB); and (ii) extrapulmonary TB, or disease affecting sites including lymph nodes, pleura, meninges, pericardia, peritoneum, spine, intestine, genitourinary tract, larynx, bone and joints, and skin.

1.1.2 Bacteriological results

“Smear-positive” or “smear-negative” is the most useful bacteriological classification of pulmonary cases because it correlates with infectiousness. In settings where culture facilities

are available, the results of culture are included in the bacteriological classification. Under most programmatic conditions – when only microscopy laboratory services are available and when diagnostic criteria are properly applied – smear-positive cases represent more than 65% of the total number of cases of pulmonary TB in adults, and 50% or more of all TB cases (although those proportions may be altered in settings with high prevalence of HIV infection).

A patient with both pulmonary and extrapulmonary TB is classified as a case of pulmonary TB.

1.1.3 Severity of disease

Bacillary load, extent of disease and anatomical site are factors that determine the severity of TB disease, and consequently its appropriate treatment. A case of pulmonary TB is classified as severe if parenchymal involvement is extensive. Miliary disseminated TB is also considered severe. Involvement of an anatomical site results in classification as severe disease if there is a significant acute threat to life (e.g. pericardial TB), a risk of subsequent severe handicap (e.g. spinal TB) or both (e.g. meningeal TB).

The following forms of extrapulmonary TB are classified as severe: meningeal, pericardial, peritoneal, bilateral or extensive pleural effusion, spinal, intestinal and genitourinary. TB of the lymph nodes, unilateral pleural effusion, bone (excluding spine), peripheral joint and skin is classified as less severe.

1.2 Case detection of drug-resistant tuberculosis

Programmatic strategies for the management of drug-resistant TB aim to identify patients and initiate adequate treatment for drug-resistant cases in a timely manner. Prompt identification and initiation of adequate treatment gives a better chance of cure for patients, provides the best infection control measure, and prevents the acquisition of further resistance and progression to a chronic state of permanent lung damage.

WHO recommends that programmes have population-representative data of drug resistance surveillance (DRS) for new patients, for the different categories of re-treatment patients (failure after Category I, failure after re-treatment, default and relapse) and for other high-risk groups (see Chapter 2). Designing an effective case-finding strategy depends on this information. Availability of DRS data for the different groups also enables calculation of the number of patients who should enter the programme; this in turn greatly facilitates programme planning and drug procurement (see also Chapter 14).

Some programmes may not have sufficient laboratory capacity to provide drug susceptibility testing (DST) of all patients. Where targeted DST surveys identify a risk group or groups of patients with a high proportion of MDR-TB (which may exceed 80%), the use of Category IV regimens in all patients in that group is justified.

The three risk groups commonly considered for direct enrolment for a Category IV regimen are:

- Category II failures (chronic TB cases);
- TB patients who are close contacts of MDR-TB cases;
- Category I failures who received a full course of treatment.

The proportion of MDR-TB in these three groups may vary considerably. It is therefore important to confirm MDR-TB through the use of DST (to, at least, isoniazid and rifampicin) for all patients who start a Category IV regimen.

In most settings, other groups are unlikely to have rates of MDR-TB sufficiently high to warrant entry into a drug-resistant TB treatment regimen without confirmation of MDR-TB by DST (Box 1.1).

BOX 1.1

DEFINITIONS OF MULTIDRUG-RESISTANT TUBERCULOSIS AND EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS

- **MDR-TB.** Tuberculosis with resistance to, at least, isoniazid, and rifampicin.
- **XDR-TB.** Tuberculosis with resistance to, at least, isoniazid and rifampicin **and** to any of the fluoroquinolones **and** to one of the following injectable drugs: amikacin, capreomycin, kanamycin.

1.3 Case detection of tuberculosis and human immunodeficiency virus

Important differences exist in the diagnosis of TB in HIV-prevalent settings and in settings of low HIV prevalence. HIV alters the clinical pattern of TB and complicates its diagnosis.

Infection with HIV increases the risk of progression of recent *M. tuberculosis* infection and of reactivation of latent *M. tuberculosis* infection by 5–15% annually, depending on the degree of immune deficiency. It also increases the rate of recurrence of TB, both relapse (reactivation of latent TB) and reinfection (newly acquired infection). HIV is responsible for a large increase in the proportion of patients with smear-negative pulmonary and extrapulmonary TB. These patients have inferior treatment outcomes, including excessive early mortality, compared with HIV-positive, smear-positive pulmonary TB patients. Tackling this problem requires rapid diagnosis of smear-negative pulmonary and extrapulmonary TB in settings with high HIV prevalence.

Effect of HIV on TB. HIV infection causes reduced immune competence and the consequent loss of ability to prevent the spread of the tubercle bacilli from localized granulomas (due to a decline in the number of CD4+ T cells). Rapid progression from initial infection to TB disease may also occur in markedly immunosuppressed patients. Patients with active TB who are HIV-positive have a higher risk of dying from TB than those without HIV.

In the early stages of HIV infection, before host immunity is significantly compromised, patients with TB have the typical symptoms of TB, and smear microscopy is usually positive.

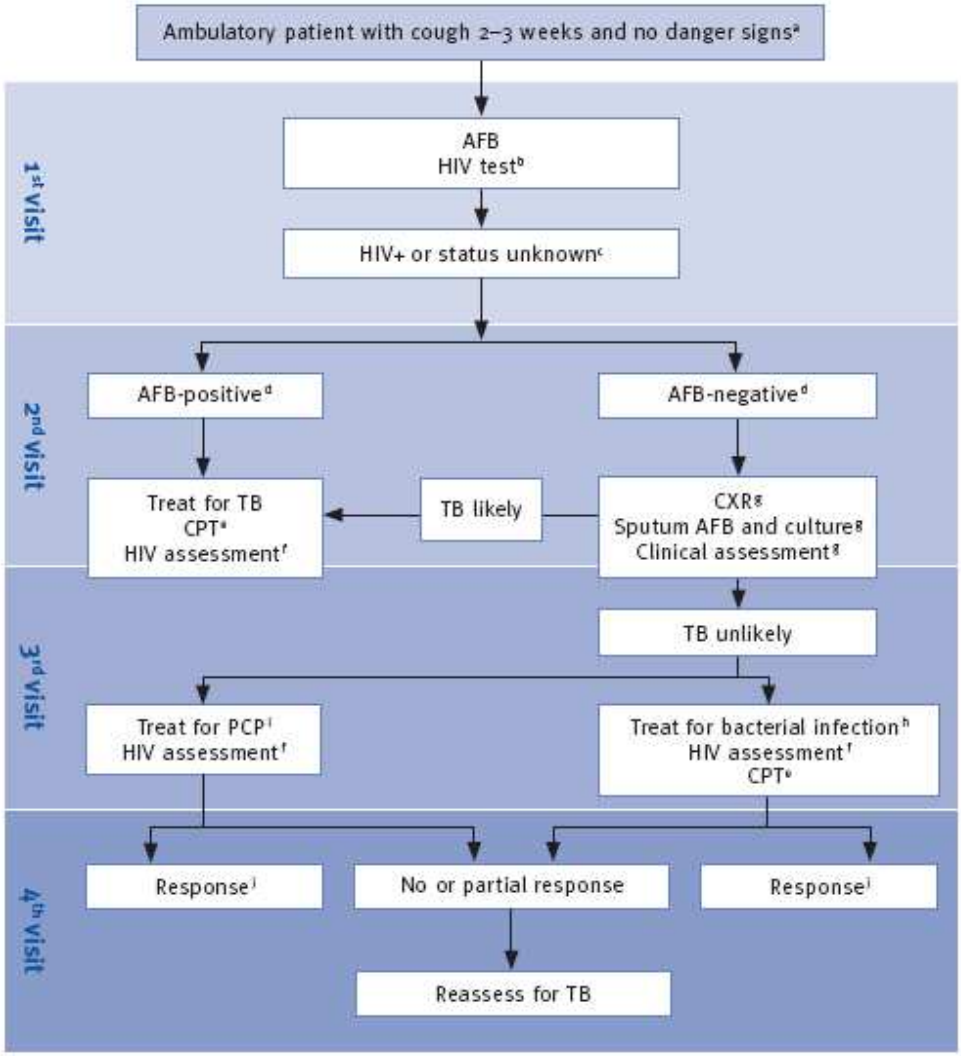
With more advanced HIV infection and compromised immune status, TB symptoms are atypical and the smear is often negative. Paucibacillary (scanty) smears are also more frequent in HIV-infected TB patients. HIV-positive patients with smear-negative TB are more likely to die during or before diagnosis than HIV-negative smear-positive patients.

Radiography. The use of chest radiography to diagnose pulmonary TB may be compromised by poor film quality, low specificity and difficulties with interpretation. HIV infection further diminishes the reliability of chest radiographs for the diagnosis of pulmonary TB because the disease commonly presents with an atypical pattern. Furthermore, the chest radiograph may be normal in a proportion of HIV-infected patients with sputum culture-positive TB (observed in up to 14% of such cases). However, chest radiography remains an important adjunct to the diagnosis of smear-negative pulmonary TB in people living with HIV (PLHIV).

Diagnostic algorithms. Algorithms for the diagnosis of TB in ambulatory patients in HIV-prevalent settings and in seriously ill HIV-positive patients are provided below (Figures 1.2 and 1.3).

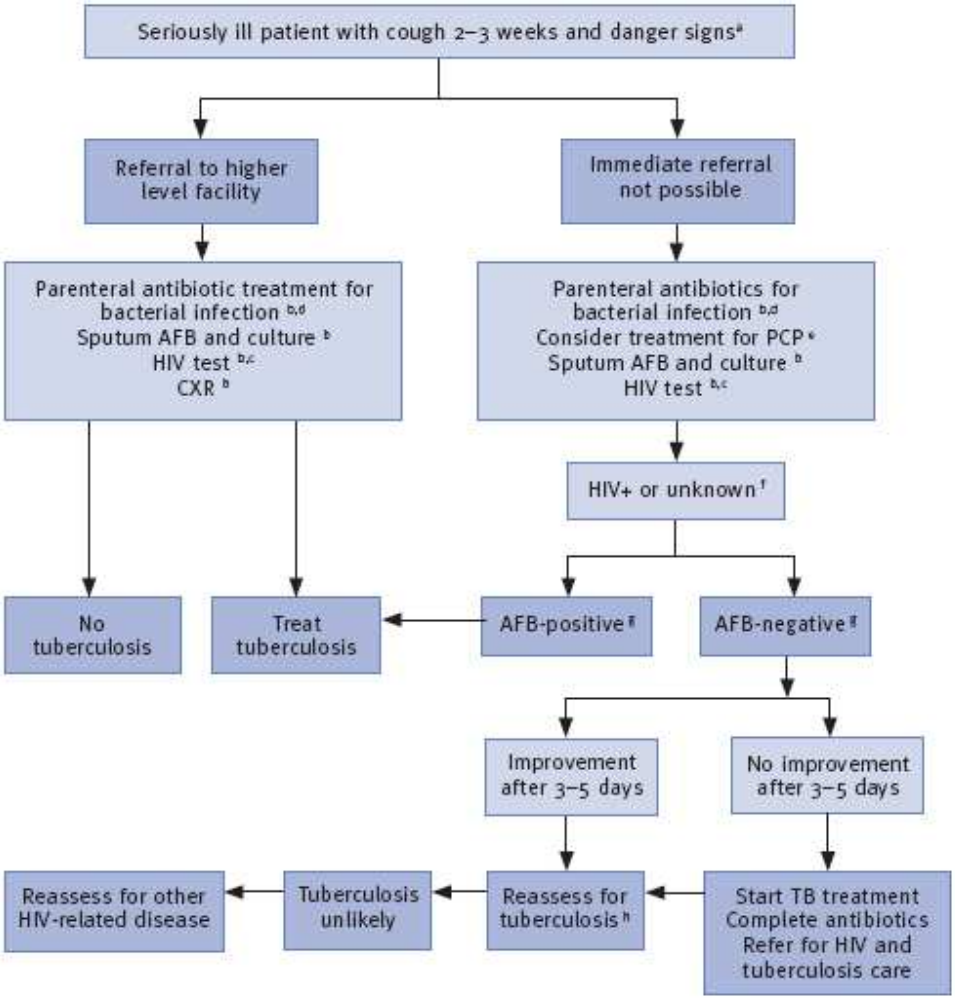
The diagnosis of smear-negative pulmonary TB is particularly difficult among HIV-positive patients, and use of the algorithm is therefore recommended.

FIGURE 1.2 ALGORITHM FOR THE DIAGNOSIS OF TUBERCULOSIS IN AMBULATORY HIV-POSITIVE PATIENTS



[a] The danger signs include any one of: respiratory rate >30/minute, fever >39 °C, pulse rate >120/min and unable to walk unaided.
[b] For countries with adult HIV prevalence rate ≥1% or prevalence rate of HIV among tuberculosis patients ≥5%.
[c] In the absence of HIV testing, classifying HIV status unknown as HIV-positive depends on clinical assessment or national and/or local policy.
[d] AFB-positive is defined as at least one positive and AFB-negative as two or more negative smears.
[e] CPT = Co-trimoxazole preventive therapy.
[f] HIV assessment includes HIV clinical staging, determination of CD_4 count if available and referral for HIV care.
[g] The investigations within the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnosis.
[h] Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.
[i] PCP: *Pneumocystis carinii* pneumonia, also known as *Pneumocystis jirovecii* pneumonia.
[j] Advise to return for reassessment if symptoms recur.

FIGURE 1.3 ALGORITHM FOR THE DIAGNOSIS OF TUBERCULOSIS IN SERIOUSLY ILL HIV-POSITIVE PATIENTS



[a] The danger signs include any one of: respiratory rate >30/minute, fever >39 °C, pulse rate >120/min and unable to walk unaided.
[b] The investigations within the box should be done at the same time wherever possible in order to decrease the number of visits and speed up the diagnosis.
[c] For countries with adult HIV prevalence rate ≥1% or prevalence rate of HIV among tuberculosis patients ≥5%.
[d] Antibiotics (except fluoroquinolones) to cover both typical and atypical bacteria should be considered.
[e] PCP: *Pneumocystis carinii* pneumonia, also known as *Pneumocystis jirovecii* pneumonia.
[f] In the absence of HIV testing, classifying HIV status unknown as HIV-positive depends on clinical assessment or national and/or local policy.
[g] AFB-positive is defined as at least one positive and AFB-negative as two or more negative smears.
[h] Reassessment for tuberculosis includes AFB examination and clinical assessment.

The algorithm for HIV-negative patients (Figure 1.1) includes treatment with a course of broad-spectrum antibiotics to exclude infections other than TB, and to improve the specificity of the diagnosis.

The result of antibiotic treatment is not affected by HIV status. However, patients with TB may lose their respiratory symptoms after a course of antibiotics.

The specific aspects of TB diagnosis in HIV-prevalent settings are that:

- the clinical assessment of the seriousness of disease is taken into account;
- special efforts to avoid delay in establishing the diagnosis should be made;
- the use of antibiotics (for clinical reasons) is not a step in the diagnostic process;
- all available investigations, such as chest radiography, culture of sputum and specimen culture for cases of extrapulmonary TB, should be carried out as soon as possible.

WHO guidelines

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Chapter 2 Treatment of tuberculosis patients

2.1 Standardized regimens

The standardized regimens for anti-TB treatment recommended by WHO include five essential medicines designated as “first line”: isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S). Table 2.1 shows the recommended doses for adults and children.

TABLE 2.1 RECOMMENDED DOSES OF FIRST-LINE ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN[a]

Drug	Recommended dose			
	Daily		Three times weekly	
	Dose and range (mg/kg body weight)	Maximum (mg)	Dose and range (mg/kg body weight)	Daily maximum (mg)
isoniazid	5 (4–6)	300	10 (8–12)	–
rifampicin	10 (8–12)	600	10 (8–12)	600
pyrazinamide	25 (20–30)	–	35 (30–40)	–
ethambutol	children 20 (15–25) adults 15 (15–20)	–	30 (25–35)	–
streptomycin	15 (12–18)	–	15 (12–18)	–

[a] Adapted from *Treatment of tuberculosis: guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

For treatment purposes, patients are categorized as previously untreated (categories I and III) and previously treated (categories II and IV). Tables 2.2 and 2.3 further define these categories.

WHO recommends the use of fixed-dose combinations (FDCs) of drugs for the treatment of all TB patients. Several advantages of FDCs over individual medicines (or single-drug formulations) have been identified:

- prescription errors are likely to be less frequent;
- fewer tablets need to be ingested, which may encourage adherence to treatment;
- patients cannot select which medicines to take (when treatment is not observed).

Poor bioavailability of rifampicin has been found in some FDCs. The use of drug combinations of assured quality (including proven bioavailability) is essential; these medicines may be obtained through the Global Drug Facility (GDF).

2.1.1 Children

The recommended daily dose of ethambutol is higher in children (20 mg/kg) than in adults (15 mg/kg) because the pharmacokinetics are different (peak serum ethambutol concentrations are lower in children than in adults receiving the same mg/kg dose). Although ethambutol was frequently omitted from regimens for children in the past, owing in part to concerns about the difficulty of monitoring for toxicity (particularly for optic neuritis) in young children, a literature review indicates that ethambutol is safe in children at a dose of 20 mg/kg (range 15–25 mg/kg) daily. Streptomycin should be avoided when possible in children because the injections are painful, and irreversible auditory nerve damage may occur. The use of streptomycin in children is mainly reserved for the first two months of treatment of TB meningitis.

2.1.2 New cases

For treatment of new cases of pulmonary or extrapulmonary TB, WHO recommends a standardized regimen consisting of two phases. The initial (intensive) phase uses four drugs

(rifampicin, isoniazid, pyrazinamide and ethambutol) administered for two months. This is followed by a continuation phase with two drugs (rifampicin and isoniazid) for four months or, exceptionally, with two drugs (isoniazid and ethambutol) for six months when adherence to treatment with rifampicin cannot be ensured (Table 2.2).

TABLE 2.2 RECOMMENDED TREATMENT REGIMENS FOR NEW CASES OF TUBERCULOSIS[a]

Patient treatment category	Patient diagnostic category	Treatment regimens[b]	
		Initial phase	Continuation phase
I	New smear-positive patients, new smear-negative patients with extensive parenchymal involvement, concomitant HIV-related diseases or severe forms of extrapulmonary TB	**Preferred** 2 HRZE[c]	**Preferred** 4 HR $4\ (HR)_3$
		Optional 2 HRZE	**Optional** 6 HE
		Optional[d] $2\ (HRZE)_3$	**Optional** $4\ (HR)_3$
III	New smear-negative pulmonary TB (other than in Category I) and less severe forms of extrapulmonary TB	**Preferred** 2 HRZE[e]	**Preferred** 4 HR $4\ (HR)_3$
		Optional 2 HRZE	**Optional** 6 HE
		Optional $2\ (HRZE)_3$	**Optional** $4\ (HR)_3$

[a] Adapted from *Treatment of tuberculosis: guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

[b] Numbers preceding regimens indicate the length of treatment in months. Subscript numbers following regimens indicate the frequency of administration per week. When no subscript numbers are given, the regimen is daily.

[c] Streptomycin may be used instead of ethambutol and it should replace ethambutol in tuberculous meningitis.

[d] The thrice weekly treatment was less effective than daily treatment, as measured by conversion rates at 2 months, with a suggestion of less favourable outcomes overall; although the difference in outcome from the 8-month daily regimen was negligible (Jindani A, Nunn AJ, Enarson DE. Two 8-month regimens of chemotherapy for treatment of newly diagnosed pulmonary tuberculosis: international multi-centre randomized trial. *Lancet*, 2004, 364:1244–1251.).

[e] Ethambutol in the initial phase may be omitted for patients with limited, non-cavitary, smear-negative pulmonary TB who are known to be HIV-negative, patients with less severe forms of extrapulmonary TB and patients with known susceptible strains.

Patients with a large bacillary load (sputum smear-positive pulmonary TB and many HIV-infected patients with smear-negative pulmonary TB) have an increased risk of selecting resistant bacilli. Short-course chemotherapy regimens with four drugs (HRZE) in the initial phase reduce this risk. Such regimens are highly effective in patients with susceptible bacilli.

The same four-drug regimen, including ethambutol, should be used during the initial phase of treatment for patients with smear-positive pulmonary, smear-negative pulmonary and extrapulmonary TB.

HIV-negative patients with smear-negative or extrapulmonary TB that is fully drug-susceptible have little risk of selecting resistant bacilli because their lesions generally harbour fewer bacilli. Such cases may be treated with a three-drug regimen (RHZ). However, given that initial resistance to isoniazid is common in many settings, that recent DST surveillance data may not be available and that the HIV status of many TB patients is unknown, this three-drug regimen is not recommended.

Supervised daily administration of medicines in the initial phase of treatment of all new cases is recommended. Since outcomes for ethambutol are poorer in those with HIV infection, the preferred option is RH rather than EH for HIV-positive patients.

The preferred continuation-phase regimen is four months of rifampicin and isoniazid (4RH) administered daily or three times weekly. The main advantage of this regimen is the low rate of treatment failure and relapse for patients with fully susceptible TB or TB with initial resistance to isoniazid. The use of rifampicin requires measures to support patients to adhere to treatment and to prevent the development of rifampicin resistance. Daily treatment may be appropriate if the patient is hospitalized, or if the treatment supporter (health worker, neighbour, community or family member) is able to provide care close to the patient's home. It is also easier for the patient to remember to take the medicine (if a treatment supporter is

not available), and the consequence of a missed dose is less detrimental. Three times weekly therapy *always requires direct observation* and if taken regularly, its effectiveness is similar to that of daily therapy. WHO does not recommended a twice-weekly regimen.

In the continuation phase, a self-administered regimen comprising daily treatment with six months of isoniazid and ethambutol (6HE) is an option if adherence to treatment with isoniazid and rifampicin (HR) cannot be ensured; for example, in mobile populations and for patients with very limited access to health care. However, in a comparative international multicentre clinical trial, 6HE was found to be inferior to the 4HR continuation phase regimen, with a significantly higher unfavourable outcome (failure or relapse) at 12 months after the end of chemotherapy. The proportions with unfavourable outcomes were 10% for the 2HRZE/6HE regimen (initial and continuation phases administered daily), 14% for $2(HRZE)_3/6HE$ (initial phase administered three times weekly) and 5% for 2HRZE/4HR.

Pregnancy and lactation. Of the first-line drugs, isoniazid, rifampicin and ethambutol may be given safely during pregnancy. Streptomycin may cause ototoxicity in the fetus and is contraindicated. Most anti-TB drugs appear in low concentrations in breast milk at levels that do not produce toxicity in infants. Breastfeeding is not contraindicated.

2.1.3 Previously treated cases

Drug resistance is more likely to develop in previously treated patients (i.e. patients who have been treated for longer than one month) who continued to be or who became sputum smear (or culture) positive. Ideally, all previously treated patients should be assessed for drug susceptibility before initiating chemotherapy. However, in settings where access to quality-assured culture and DST is limited, WHO recommends a standardized regimen for previously treated cases. Table 2.3 shows the possible therapeutic options for previously treated patients (Category II regimen).

The standard re-treatment regimen consists of:

- *five drugs in the initial phase* (rifampicin, isoniazid, pyrazinamide, ethambutol and streptomycin). The initial phase is administered for three months, with all five drugs administered for the first two months. Streptomycin is discontinued after two months, and the four remaining drugs are given in the third month. WHO recommends daily administration of drugs in the initial phase;
- *three drugs in the continuation phase* (rifampicin, isoniazid and ethambutol). The continuation phase is administered for five months, daily or intermittently, three times a week.

TABLE 2.3 - Recommended treatment regimens for previously treated patients (Re-treatment regimens)[a]

Patient diagnostic category	TB patient diagnostic category	TB treatment regimens	
		Initial phase	**Continuation phase**
II	Relapses Treatment after default	**Preferred** 2 HRZES/ 1 HRZE	**Preferred** 5 HRE
		Optional 2 $(HRZES)_3$/ 1 $(HRZE)_3$	**Optional** 5 $(HRE)_3$
II	Treatment failure of Category I In settings where: Representative DRS data show low rates of MDR-TB or individualised DST show drug-susceptible disease **or** In settings of: • Poor programme performance; • Absence of representative DRS data and/ or capacity for DST of cases; • Insufficient resources to implement Category IV treatment	**Preferred** 2 HRZES/ 1 HRZE	**Preferred** 5 HRE
		Optional 2 $(HRZES)_3$/ 1 $(HRZE)_3$	**Optional** 5 $(HRE)_3$
IV	Treatment failure of Category I In settings with: • Adequate programme performance; • Representative DRS data showing high rates of MDR-TB and/ or capacity for DST of cases; • Availability of 2nd line drugs	Specially designed standardized[b] or individualised regimens with the use of 2nd line drugs	
IV	Still smear- or culture-positive after supervised re-treatment regimen); proven or suspect MDR-TB cases[c]	Specially designed standardized or individualised regimens with the use of 2nd line drugs.	

DRS = drug resistance surveillance, DST = susceptibility testing; MDR-TB = multidrug-resistant tuberculosis

[a] Adapted from Treatment of tuberculosis: guidelines for national programmes, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).
[b] It is recommended that standardized regimens are based on representative DRS data from patients categories or groups
[c] Drug susceptibility testing is recommended for patients who are contacts of known MDR-TB cases

This standardized regimen can cure patients excreting bacilli fully sensitive or resistant to isoniazid and/or streptomycin. It should not be used in failures of the Category I regimen, who have a high probability of MDR-TB. This applies particularly to patients who failed after directly observed therapy (DOT) and where rifampicin was included in the

continuation phase. Patients who fail treatment are at much higher risk of developing anti-TB drug resistance. However, while failure in a patient whose treatment has been directly observed may be attributable to an initial resistance to the drugs, failure in situations where treatment has not been directly observed may be the result of poor treatment adherence, chaotic treatment or insufficient drug dosages.

The Category II standardized regimen has poor results in MDR-TB cases (less than 50% cure rate) and may result in the acquisition of additional resistance to those drugs that were still effective at the start of treatment (e.g. E and/or Z). Countries with a high proportion of MDR-TB among failures of the Category I regimen should consider treating such cases with a regimen consisting of second-line drugs (see Chapter 11).

Streptomycin should be administered by injection using disposable (single use) or sterile (reusable) needles and syringes. It should not be used in settings where the use of disposable or sterile needles and syringes is not assured. The use of inadequately sterilized reusable syringes and needles carries a risk of transmission of HIV and other bloodborne pathogens.

Adverse effects of anti-TB drugs

A minority of TB patients (0.7–14%) treated with Category I or Category II regimens experience adverse effects. These include:

- major adverse effects giving rise to serious health hazards and requiring discontinuation of anti-TB treatment;

- minor side-effects causing relatively little discomfort and often responding to symptomatic or simple treatment; they may occasionally persist for the duration of anti-TB treatment.

Details on the most important and frequent side-effects are provided in *Treatment of tuberculosis: guidelines for national programmes*.

Inadequate management of adverse effects is likely to contribute to irregular treatment and default. The NTP should implement a pharmacovigilance system.

2.2 Treatment of drug-resistant tuberculosis

Patients in whom drug-resistant TB is diagnosed and who require treatment with second-line drugs are classified as WHO TB diagnostic Category IV and require regimens termed "Category IV regimens". This section provides guidance on the strategy options, including standardized, empirical and individualized approaches, for treating drug-resistant TB. A description of drugs, doses and coding of treatment regimens is provided in *Guidelines for the programmatic management of drug-resistant tuberculosis*.

XDR-TB is a subset of MDR-TB that shows additional resistance to second-line drugs. Patients with MDR-TB require special attention to avoid the development of XDR-TB, and those who have XDR-TB require rigorous treatment, with the frequent addition of third-line agents (Category V drugs). Available evidence on XDR-TB and its treatment is limited, but

experience in some well-controlled settings shows significantly lower treatment success rates compared with those for MDR-TB cases.

2.2.1 Treatment strategies

Strategies for treatment should be developed on the basis of previous assessment of both the drug resistance survey data and the frequency of use of anti-TB drugs in the country. A programme that plans to introduce a treatment strategy for drug-resistant TB should be familiar with the prevalence of drug resistance in new patients as well as in different groups of re-treatment cases (failures, relapse, return after default and chronic cases). It is essential to determine which second-line anti-TB drugs have been used, and with what frequency, in the setting served by the programme, as well as the use by both private and public providers. Second-line anti-TB drugs that have been used only rarely are likely to be effective in regimens for drug-resistant TB. Second-line drugs that have been used extensively are less likely to be effective in patients with resistant strains.

Some programmes may need to design strategies based on limited data only, as treatment for many patients should not be delayed until the full essential assessment information becomes available. In such cases, the programme can still follow the basic principles for designing an effective regimen and continue to collect the information described in this section.

The different options for treatment strategies include standardized treatment, empirical treatment and individualized treatment. No treatment strategy can fit all situations, and the choice between these strategies will depend on many factors, including the operational context and laboratory capacity.

2.2.2 Regimen design

The following basic principles are involved in regimen design.

- Regimens should be based on the history of medicines taken by the patient.
- Drugs commonly used in the country and prevalence of resistance to first-line and second-line drugs should be taken into consideration when designing a regimen.
- Regimens should consist of at least four drugs with either certain or highly probable effectiveness. In the case of unclear evidence about its effectiveness, a drug can be part of the regimen but it should not be depended upon for success. More than four drugs may be started if the susceptibility pattern is unknown, if effectiveness is questionable for one or several agents or if extensive, bilateral pulmonary disease is present.
- Drugs are administered at least six days per week. When possible, pyrazinamide, ethambutol and fluoroquinolones should be given once per day because the high peaks attained in once-a-day dosing may be more efficacious. Once-a-day dosing is permissible for other second-line drugs, depending on patient tolerance. However ethionamide/protionamide, cycloserine and *P*-aminosalicylic acid have traditionally been given in divided doses during the day.
- The drug dosage should be determined by body weight. A suggested weight-based dosing scheme is shown in Table 2.1.
- An injectable agent (an aminoglycoside or capreomycin) is used for a minimum of six months or for four months after culture conversion, whichever is longer.
- Each dose is given as DOT throughout the treatment, and a treatment card is marked for each observed dose.

- DST, when available and from a reliable laboratory, should be used to guide therapy. However, the quality and comparability of results in DST of some first-line and most of the second-line anti-TB drugs have not been fully assessed, and DST does not predict the effectiveness of a drug with complete certainty. Despite these limitations, regimens should include at least four drugs highly likely to be effective based on DST and/or drug history of the patient.
- Pyrazinamide may be used for the entire treatment if it is judged to be effective. Many MDR-TB patients have chronically inflamed lungs, which (theoretically) produce the acidic environment in which pyrazinamide is active.

2.2.3 Duration of treatment

The recommended duration of treatment is guided by smear and culture conversion. The minimal recommendation is that treatment lasts for at least 18 months after culture conversion; extension to 24 months may be indicated in chronic cases with extensive pulmonary damage.

Treatment of drug-resistant TB is a complex health intervention, and no single strategy will fit all situations. Programme managers need to consider the epidemiological, financial and operational factors when deciding which strategy to use.

2.3 Treatment of tuberculosis in HIV-infected patients

For HIV-infected patients with active TB disease, the first priority is to initiate standardized anti-TB treatment. The optimal time for starting ART in these cases is not known and the decision is based on risk–benefit considerations.

The principles of anti-TB treatment are the same irrespective of HIV status. Although ethambutol and isoniazid are included in recommendations for the continuation phase, short-course regimens that contain rifampicin throughout have better outcome, and reduce the risk of TB recurrence.

The use of thioacetazone is ***contraindicated*** in HIV-infected individuals because of the risk of fatal hypersensitivity reactions and is discouraged by WHO because of the risk of severe toxicity. Ethambutol should replace thioacetazone, especially in areas where HIV is prevalent.

2.3.1 Outcomes of anti-TB treatment

Without adequate treatment, TB in HIV-positive patients is rapidly fatal, usually within months. Among treated TB patients, death rates are higher in HIV-positive than in HIV-negative patients (in some settings up to one third of those treated). Case fatality is higher in HIV-positive patients with smear-negative pulmonary TB, as these patients are generally more immunosuppressed than those with smear-positive TB. The risk of TB recurrence is greater in HIV-positive TB patients than in those who are HIV-negative. The case-fatality rate is reduced in patients treated with rifampicin throughout and who receive concurrent treatment against HIV, including with co-trimoxazole preventive therapy (CPT) and ART.

TABLE 3.1 DEFINITIONS OF TREATMENT OUTCOMES[a]

Cured	A patient who was initially culture or sputum smear microscopy at the beginning of the treatment but who was smear-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A patient who completed treatment but who did not meet the criteria to be classified as a cure or a treatment failure. This definition applies to pulmonary smear-positive and smear-negative patients and to patients with extrapulmonary disease.
Treatment failure	(i) A new patient who is culture or sputum smear microscopy positive at five months *or* later during treatment, or who is switched to Category IV treatment because sputum culture revealed MDR-TB; (ii) A previously-treated patient who is culture or sputum smear microscopy positive at the end of the re-treatment regimen or who is switched to Category IV treatment because sputum culture revealed MDR-TB.
Died	A patient who died from any cause during the course of treatment.
Defaulted	A patient whose treatment was interrupted for two consecutive months or more.
Transferred out	A patient who was transferred to a health facility in another basic management unit and for whom the treatment outcome is not known.
Successfully treated	A patient who was cured *or* who completed treatment.

[a] Source: *Revised TB recording and reporting forms and registers – version 2006*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.373).

2.3.2 HIV testing, treatment and care of TB patients

Tuberculosis is often the first clinical indication that someone has underlying HIV infection, and it is therefore important to offer all TB patients an HIV test. As such, TB programmes can be an extremely important entry point to HIV care and treatment, including CPT, and often ART.

2.3.3 Provision of co-trimoxazole preventive therapy

Administering prophylactic co-trimoxazole may prevent *Pneumocystis jirovecii* and bacterial infections in HIV-positive TB patients. CPT substantially reduces mortality in HIV-positive TB patients (by up to 48% in the WHO African Region). For TB patients, CPT should be initiated as soon as possible, irrespective of the CD4 cell count, and given throughout anti-

TB treatment; continuation after treatment is completed should be considered in accordance with national guidelines. TB and HIV control programmes should establish a system for provision of CPT to eligible PLHIV who have active TB.

2.3.4 Provision of antiretroviral therapy

In this rapidly evolving field, updated information and guidance is provided by WHO.[1] ART is recommended for all HIV-positive patients with extrapulmonary TB (Stage 4) and for all those with pulmonary TB (Stage 3) unless the CD4 cell count exceeds 350 cells/mm3. ART reduces both case-fatality rates and the incidence of TB and recurrent TB. If measurement of the CD4 cell count is not possible, ART should be initiated for stages 3 and 4 once the patient has stabilized on anti-TB treatment, generally after 2–8 weeks of treatment.

The optimal time to start ART is not clear-cut. Early initiation of ART within a few weeks of starting anti-TB treatment is associated with a high burden of tablets to ingest, which may discourage treatment adherence, and may be complicated by adverse effects, drug–drug interactions and immune reconstitution inflammatory syndrome (IRIS). However, since much of the case fatality in HIV-positive TB patients occurs in the first two months of anti-TB treatment, delayed initiation of ART may reduce its potential benefits.

[1] http://www.who.int/HIV

TABLE 2.4 INITIATING FIRST-LINE ANTIRETROVIRAL THERAPY IN RELATION TO STARTING ANTI-TB TREATMENT[a]

CD4 cell count	ART recommendations	Timing of ART in relation to the start of anti-TB treatment
CD4 <200 cells/mm_3	Recommend ART[b]	Between 2 and 8 weeks[c]
CD4 200–350 cells/mm_3	Recommend ART	After 8 weeks
CD4 >350 cells/mm_3	Defer ART[d]	Re-evaluate patient at 8 weeks and at the end of anti-TB treatment
CD4 not available	Recommend ART[e]	Between 2 and 8 weeks

[a] Adapted from *Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach*, 6th revision. Geneva, World Health Organization, 2006.
[b] A regimen containing efavirenz is the preferred first-line regimen; alternative regimens include nevirapine (NVP) and triple nucleoside reverse transcriptase inhibitors based on regimens using tenofovir disoproxil fumarate or abacavir. For NVP-containing regimens, alanine aminotransferase should be checked at 4, 8 and 12 weeks, and directed by symptoms thereafter.
[c] Start ART as soon as anti-TB treatment is tolerated.
[d] If other non-TB stage 3 or 4 events are present, start ART.
[e] For some TB diagnoses that generally respond well to anti-TB treatment (i.e. TB of the lymph nodes, uncomplicated pleural effusion), consider deferring ART.

Selection of drugs

- Rifampicin-containing regimens are recommended for treatment of TB in HIV-infected patients. However, rifampicin induces the activity of hepatic cytochrome P450, leading to subtherapeutic concentrations of some antiretroviral drugs.
- Efavirenz-containing regimens are the recommended first-line ART regimens for TB patients, since interactions with anti-TB drugs are minimal. Efavirenz is potentially teratogenic and is ***contraindicated*** for women of childbearing potential without adequate contraception or for those who are in the first trimester of pregnancy.
- Nevirapine is an alternative to efavirenz, but in combination with rifampicin poses an increased risk of hepatotoxicity. If used, clinical and laboratory monitoring are recommended. The use of triple nucleoside antiretroviral regimens is emerging as an additional alternative.

- When rifabutin is used in place of rifampicin, protease inhibitor-containing regimens may be administered with rifabutin dose adjustment. However, rifabutin may not be available or accessible, and it is costly.

2.3.5 Tuberculosis in patients already receiving antiretroviral therapy

Patients in whom TB is diagnosed while receiving ART should start anti-TB treatment immediately to assess whether the development of active TB reflects a failure of ART that would require changing the ART regimen. Adjustments of ART may be needed for patients who develop active TB within six months of the start of first-line or second-line ART.

Within six months of initiating ART. If an episode of TB occurs during the first six months following the initiation of ART, this should not be considered a treatment failure event, and the ART regimen should be adjusted for co-administration with rifampicin-containing regimens.

After six months of initiating ART. The development of an episode of pulmonary TB after six months of ART, without other clinical and immunological evidence of HIV disease progression, should not be regarded as representing ART failure. If other clinical and immunological evidence of HIV disease progression is present, the episode of pulmonary disease should be regarded as representing an episode of ART failure. The development of extrapulmonary TB (after six months) should also be considered as indicating ART failure.

2.3.6 Immune reconstitution inflammatory syndrome

IRIS is a temporary exacerbation of symptoms and/or radiographic signs of TB occurring soon after the start of treatment with ART and anti-TB drugs. The syndrome most commonly presents with fever and worsening of pre-existing respiratory disease or lymphadenopathy after initial improvement on anti-TB treatment in patients who have started on ART in the past three months, although it may occur within five days. It is similar to, but more frequent than, the paradoxical reactions seen in immunocompetent patients on anti-TB therapy.

IRIS appears to be more common if ART is started early in the course of anti-TB treatment. The diagnosis is clinical and the differential diagnosis includes adverse effects of ART, failure of TB treatment caused by drug resistance or poor adherence, failure of ART, or other underlying infection. Most cases resolve without any intervention, and ART may be safely continued. Occasionally, serious reactions such as tracheal compression caused by massive adenopathy or respiratory difficulty may require the use of corticosteroids.

TB-related IRIS may present as one of two main syndromes: (i) a paradoxical reaction after the start of ART in patients receiving treatment for TB ("paradoxical TB-IRIS"); or (ii) an exaggerated new presentation of TB that is "unmasked" in the weeks following initiation of ART.

2.4 Treatment support

For anti-TB therapy to be effective, appropriate drugs should be used in appropriate doses and ingested correctly for the appropriate length of time. Adherence to treatment is therefore

crucial to completing treatment and achieving cure. Services providing TB care should offer full support to patients to ensure that treatment will be completed.

Staff who provide TB care should identify and address factors that may make patients interrupt or stop treatment. Supervised treatment assists patients in taking their drugs regularly and in completing their treatment, thus helping to achieve cure, prevent the development of drug resistance and, by reducing disease transmission, protect the general public from TB. Supervision of treatment is meant to ensure adherence on the part of both the providers (in giving proper care and detecting treatment interruption) and the patients (in taking regular treatment). It should be carried out in a context-specific and patient-friendly manner. Depending on the local conditions, supervision may be undertaken at a health facility, in the workplace, in the community or at home. The treatment supporter should be a person acceptable to and chosen with the patient, and trained and supervised by the health services. Patient and peer support groups may help to promote adherence to treatment.

The importance and the frequency of supervision may vary, depending upon factors such as the type of drug regimen (daily or intermittent), the type of drug formulation (FDCs or individual drugs) as well as the characteristics of the patient. Actual observation of the ingestion of each dose is indispensable in the treatment of, for example, psychologically handicapped patients, prison inmates, or patients receiving second-line anti-TB drugs. It is the spirit of supporting a patient that the guaranteed intake of the full course of

treatment and ensured cure are more important than the act of observing the patient swallowing the medication.

The whole purpose of undertaking treatment observation would be lost if it were to limit access to care, turn patients away from treatment or add to their hardships. Because TB is a public health problem and its transmission poses a risk to the community, facilitating and ensuring regular intake of all the drugs by the patient is a responsibility of the health staff and of the NTP. Many NTPs now have considerable experience in identifying adherence promotion strategies that work or do not work in a given context. TB programmes should continue to strengthen patient supervision and support with the goal of achieving 100% treatment adherence rates.

Measures to facilitate patient adherence with regular and complete treatment might involve:

- a regular supply of drugs provided free of charge by the health system, preferably in FDCs, ensuring intake of all drugs;
- presentation of drugs in patient kits, to ensure that drugs for the full course of treatment are reserved for the patient at the outset of treatment;
- provision of care in a setting close to the patient's home, in order to reduce travel costs and loss of time and wages;
- appropriate patient education, including information regarding the regimen, duration and possible treatment outcomes, provided repeatedly by well-trained and considerate staff;

- provision or financing of transport and incentives such as food or hygienic packages for patients and their families, if appropriate for the context and patient profile.

Hospitalization is essential for patients in a severe clinical condition, with complications or associations requiring closer clinical monitoring. It might also be an alternative, especially during the initial phase of treatment, for a small number of patients for whom other options of ensuring treatment adherence and support are not available. However, hospitalization per se does not ensure regular drug intake or completion of the treatment.

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Chapter 3 Recording and reporting

Good recording practices are necessary for effective patient management. Assessment of programme performance and epidemiological trends provides the basis for programmatic and policy development. Effective monitoring depends on appropriate recording and reporting systems. These systems are essential to ensure high-quality TB patient care and information-sharing.

As systems becomes increasingly complex and computers become part of standard health facility equipment, NTPs are adopting electronic TB registration, which has the potential to ensure more comprehensive data entry, facilitate communication and transmission of data to other levels of the health system, and provide a more refined analysis of programme performance. (However, the electronic system is only as good as the data themselves and the accuracy of data that are manually entered.) Electronic recording and reporting follows the same principle and format as the paper-based recording and reporting system. A proper electronic system should provide a regular print-out of quarterly reports and registers to facilitate data analysis and data verification.

3.1 Recording and reporting system

The WHO TB recording and reporting system[1] is part of the general health information system (Box 3.1). It consists of detailed patient forms that are filled out at the point of care and summarized in laboratory and medical registers. These data are aggregated to prepare

[1] http://www.who.int/tb/dots/r_and_r_forms/en/index.html

quarterly reports on activities and results as well as annual management reports at the basic management unit (BMU), usually the district level, and then sent to the central level. The recording (patient registration) and reporting system is used to systematically evaluate patient progress and treatment outcomes, as well as to monitor overall programme performance (through cohort analysis).

BOX 3.1

RECORDING AND REPORTING FORMS REQUIRED BY WHO[a]

At basic management unit (BMU) level (district)

- TB laboratory register
- BMU TB register
- Quarterly report on TB case registration in BMU
- Quarterly report on TB Treatment outcomes and TB/HIV activities in BMU
- Quarterly order form for TB drugs
- Quarterly order form for laboratory supplies in BMU
- Yearly report on programme management in BMU
- Quarterly report on sputum conversion, (optional)

At BMU level (district) using routine culture and drug susceptibility testing (DST)

- TB laboratory register for culture
- TB register in BMU using routine culture and DST
- Quarterly report on TB case registration in BMU using routine culture
- Quarterly report on TB Treatment outcomes and TB/HIV activities in BMU using routine culture
- Quarterly order form for culture and DST laboratory supplies in BMU

At health facility in central, regional or peripheral level

- Request for sputum smear microscopy examination
- Request for sputum smear microscopy examination, culture, DST
- TB Treatment card
- TB Identity Card
- TB treatment referral/transfer
- Register of TB suspects (optional)
- Register of TB contacts (optional)
- Register of referred TB cases, (optional)

BMU = basic management unit; DST = drug susceptibility testing

[a] Source: *Revised TB recording and reporting forms and registers – version 2006*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.373).

3.1.1 Recording system

The recording system (patient registration) comprises: (i) laboratory registers, which record all symptomatic patients who have had a sputum smear examination; (ii) patient treatment

cards, which detail the regular intake of medication and follow-up sputum examinations; (iii) identity cards, which are kept by the patient; and (iv) BMU (district) TB registers, which list each patient starting treatment and monitor progress towards cure. Some facilities have additional registers, e.g. for TB suspects, culture results, contacts, referrals and transfers, which are adapted to country needs.

Laboratory register. The laboratory register is maintained by a laboratory technician. It records patient details by source of referral using a serial identification number. The results of the sputum smear examinations are recorded in the laboratory register either for diagnosis or for follow-up and then returned to the referring facility.

Patient treatment card. A patient treatment card is created for each TB case (smear-positive, smear-negative or extrapulmonary). It records basic epidemiological and clinical information, and the administration of drugs. The health worker uses the patient treatment card for recording treatment and for follow-up.

Identity card. An identity card is completed for every patient who starts anti-TB treatment. It records the name, age, sex, address, health facility, type of TB, regimen and dates of treatment. This card is kept by the patient.

BMU (district) TB register. The BMU TB register is used to monitor progress and treatment outcomes for all patients in the district. It provides, on one line per patient, the essential information for identification of the patient and status of case management. The register is

used by the responsible health worker to provide the district or local health officer with rapid feedback on programme performance in the district.

3.1.2 Reporting system

The reporting system consists of: (i) quarterly reports on TB case registration, which summarize the numbers of TB patients started on treatment, laboratory tests performed and HIV tests and results obtained; (ii) quarterly reports, which detail treatment outcomes and TB/HIV activities after all patients in the cohort have completed their course of treatment; (iii) quarterly order forms, which specify the required anti-TB drugs; (iv) quarterly order forms, which detail the required laboratory supplies; (v) annual reports on programme management, which describe the human resource and TB delivery service facilities as well as the contribution of the private sector and community to referral, diagnosis and treatment.

Cohort analysis. Cohort analysis refers to the systematic analysis of standard outcomes of treatment. A cohort of TB patients consists of patients registered during a certain time period, usually one quarter of a year (i.e. 1 January – 31 March, 1 April – 30 June, 1 July – 31 September and 1 October – 31 December). New sputum smear-positive pulmonary TB patients, those (the infectious cases) on re-treatment regimens, and sputum smear-negative and extrapulmonary TB patients are reported in separate cohorts.

In smear-positive pulmonary TB patients, the six standard outcomes of treatment for reporting purposes are: cure, treatment completed, treatment failure, died, default, and transfer out.

In smear-negative pulmonary TB and extrapulmonary TB patients, cure cannot be assessed because this outcome indicator depends on the results of sputum smear examination. However, outcome indicators such as treatment completed, treatment failure, died, default and transfer out should be recorded for these patients in the BMU TB Register. New and previously treated patients should also form separate cohorts. Separate cohort analysis may also be made for different types of treatment unit (e.g. public and private) or for different types of treatment supporters (e.g. health workers, community volunteers or family members). The treatment outcomes are defined in Table 3.1.

The recording and reporting system allows for individualized follow-up to help patients who do not make satisfactory progress, and for rapid managerial assessment of the overall performance of each institution, BMU (district), region or country. A robust system of accountability involving cross-checks between reports, registers and forms should minimize any risk of false reporting. Data quality audit tools standardize the cross-checks between reports, registers and forms. Data verification through cross-checking requires regular print-outs of electronic quarterly reports and registers supported by a proper paper-based archiving system.

WHO provides updated recommendations on the recording and reporting forms together with detailed instructions on how to complete them.[1]

3.2 Referral and transfer

[1] http://www.who.int/tb/dots/r_and_r_forms/en/index.html

Transfers and referrals of patients aim to improve the quality of their care in facilities offering more appropriate services or services that are more conveniently located, usually closer to the patient's home. Patients may be referred to or transferred from facilities for diagnosis, treatment or special care. Referral and transfer are distinct functions, with different follow-up and related tasks, and it is important to differentiate clearly between referral and transfer for the purposes of TB control. Transfer of patients without proper follow-up information reflects poor care management of patient movement and requires rapid correction through improved communication. Appropriate forms for referral, back-referral and transfer are therefore essential for effective information-sharing between different health-care providers involved in programme implementation.

Referral is the process of arranging the movement of a TB patient before registration in a BMU TB register for the purposes of starting treatment in a more convenient location or for diagnosis in a competent facility. The BMU referring a case should not register the patient in the TB register. However, a special referral register is helpful to monitor referrals and ensure appropriate follow up. The BMU receiving a "referred" patient is responsible for informing the referring facility about the arrival of the patient and for the care provided. A TB patient registered in a BMU TB register (i.e. a patient started on anti-TB treatment) could also be referred to another facility in the same BMU or outside the referring BMU for other (non-TB) tests or treatment (e.g. surgery, ART).

Transfer is the process of arranging the movement of a TB patient who is already registered in a BMU TB register between two BMUs, i.e. the patient has started treatment and will

continue treatment in another area with a different BMU TB register. The BMU "transferring out" a patient is responsible for reporting the treatment outcome in the quarterly report on TB treatment outcomes and TB/HIV activities, after obtaining this information from the BMU completing the details of treatment outcomes. The BMU receiving a patient "transferred-in" is responsible for informing the BMU that transferred the patient upon the arrival of the patient and on the eventual treatment outcome.

The TB treatment referral/transfer form is an individual patient form used both in case of transfer and referral. Half of the form should be returned to the originating facility upon arrival of the patient to provide feedback and ensure a successful referral.

A facility referring or transferring large numbers of patients, such as a large hospital, may use separate forms for referral and transfer and may have a specific register for referrals. Hospitals transferring patients out to another BMU are responsible for confirming that the BMU has received the patients and should collect information on the outcomes of treatment using all means possible, in order to update their BMU (district) TB register and cohort analysis.

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Chapter 4 Tuberculosis in children

4.1 Special features of tuberculosis in children

Of the estimated 8.8 million new cases of TB that occurred globally in 2005, about 1 million (11%) were children aged under 15 years. Children with TB differ from adults in their response to the disease in ways that may have important implications for the prevention, diagnosis and treatment of TB. Furthermore, children are at increased risk of progression of primary *M. tuberculosis* infection to disease, and are therefore a target group for preventive treatment. Children also develop primary TB more commonly than adults. Although bacteriological confirmation of TB should be sought whenever possible, this is often not possible in young children with pulmonary TB who usually cannot produce a sputum sample.

In the absence of HIV infection, most children with TB come within WHO TB diagnostic Category III and should be treated during the initial phase of treatment with three drugs (isoniazid, rifampicin and pyrazinamide) for two months, followed by a continuation phase of treatment with two drugs (isoniazid and rifampicin) for four months. Children are particularly liable to develop to TB meningitis and miliary TB and deserve special consideration (see the recommended treatment regimens in *Guidance for national tuberculosis programmes on the management of tuberculosis in children*).

There is an urgent need to improve the prevention, diagnosis and treatment of TB in children, by ensuring their inclusion in NTPs in line with international standards and guidelines. The *International standards for tuberculosis care* and WHO's guidelines on treatment of tuberculosis are relevant for patients of all ages, whether children or adults. The overall planning response to TB should include the response to TB/HIV and MDR-TB in children as well as in adults.

For NTPs to successfully and effectively prevent and manage TB in children, standardized approaches based on the best available evidence should be incorporated into existing NTP guidelines and strategies. The engagement of all who provide care to children (including paediatricians and other clinicians) is crucial. Reducing the burden of TB in children will require changing and improving many existing practices, such as those that relate to contact investigations. Updating the NTP recording and reporting system is necessary, in line with WHO recommendations. Operational research is essential to establish how NTPs can best ensure the delivery of effective prevention and care for childhood TB.

4.1.1 Policy changes

NTPs should be aware of two important policy changes that relate to recording and reporting and to the dosage of ethambutol.

Recording and reporting. NTPs should record and report two age groups for children (0–4 years and 5–14 years). This has considerable benefits: (i) it is crucial in ensuring the management of childhood TB as part of routine NTP activities; (ii) it is useful in ordering drugs, since child-friendly formulations are particularly important in children aged 0–4 years; (iii) it is important in monitoring of trends in these two distinct age groups, since children aged 0–4 years are the most vulnerable, and infection at these early ages indicates recent transmission; (iv) it will provide valuable and continuous information on market needs concerning child-friendly formulations of anti-TB drugs; and (v) it is consistent with age groupings used in the Integrated Management of Childhood Illness (IMCI).

Dose of ethambutol. When a child receives treatment with a regimen containing ethambutol, the revised recommended dose is 20 mg/kg (range 15–25 mg/kg) daily. A literature review indicates that ethambutol is safe in children of all ages at this dose. Ethambutol was previously often omitted from regimens for children, owing in part to concerns about optic neuritis.

4.2 Strategic approach to preventing and managing tuberculosis in children

The NTP's overall strategic approach to decrease the burden of childhood TB consists of two elements.

Prevention of TB. Measures to prevent TB involve screening children who are the household contacts of a TB case (usually an adult family member) to enable those

children found to have TB to be treated and those children not found to have TB to receive isoniazid preventive therapy (IPT).

Management of TB. Measures to manage TB involve the routine diagnosis, treatment, and recording and reporting of TB in children as part of routine NTP activities, in line with international standards and guidelines. The diagnosis and treatment of drug-resistant TB in children are complex and should be carried out at referral centres.

Chapter 8 provides recommendations for immunization with bacille Calmette–Guérin (BCG), one of the childhood vaccines administered under the Expanded Programme on Immunization.

The NTP should collaborate with child health services in implementing the strategic approach to prevention and management of TB in children. The overall context for providing high-quality care to sick children is provided by the IMCI strategy promoted by WHO and the United Nations Children's Fund (UNICEF) (see Chapter 23, section 23.2).

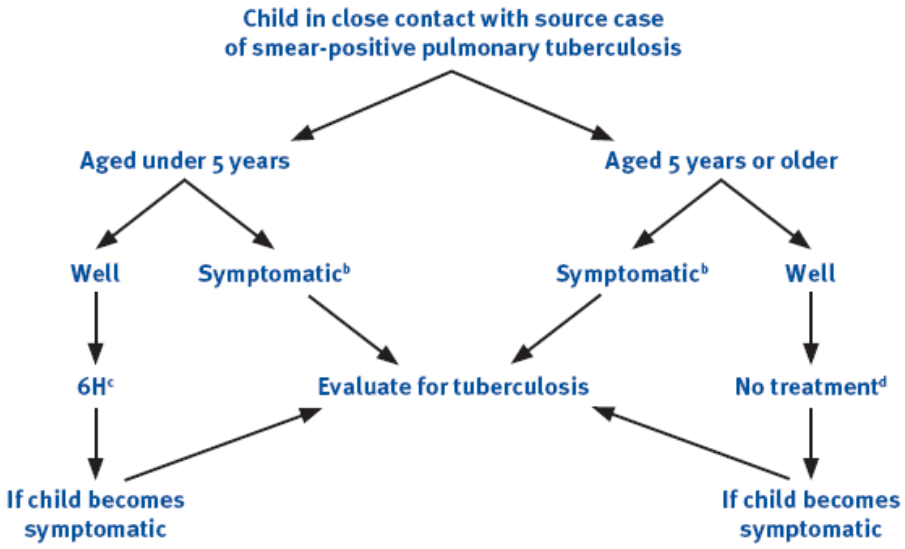
4.2.1 Prevention of tuberculosis in children

NTPs should organize a system for screening the children of household contacts of infectious pulmonary TB cases. This enables those children found to have TB to be registered and treated, and for those children not found to have TB but who are at high

risk of TB (children aged less than 5 years and all HIV-infected children) to receive IPT (i.e. daily isoniazid for at least six months).

The tuberculin skin test (TST) is the best way to detect *M. tuberculosis* infection, and chest X-ray (CXR) is the best method to screen for TB disease among contacts. These tests should be used where available to screen exposed contacts. However, tuberculin is often unavailable in low-resource settings. TST and CXR, when not readily available, should not preclude contact screening and management, as this can be conducted on the basis of simple clinical assessment (Figure 4.1).

FIGURE 4.1 APPROACH TO CONTACT MANAGEMENT WHEN CHEST X-RAY AND TUBERCULIN SKIN TEST ARE NOT READILY AVAILABLE[a]



[a] Adapted from *Guidance for national tuberculosis programmes on the management of tuberculosis in children*. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.371).
[b] If tuberculosis is suspected, refer to Part I.
[c] Isoniazid 5 mg/kg daily for 6 months.
[d] Unless the child is HIV-infected (in which case isoniazid 5 mg/kg daily for 6 months is indicated).

Special situations

- *Close contacts of MDR-TB patients*

  Children who are close contacts of MDR-TB patients should receive careful clinical follow-up for a period of at least two years. If active disease develops, prompt initiation of treatment with a regimen designed to treat MDR-TB is recommended. WHO does not recommend second-line drugs for chemoprophylaxis in MDR-TB contacts.

- *Breastfeeding infants*

  Infants who are being breastfed have a high risk of infection from mothers with smear-positive pulmonary TB and of developing TB. Infants should receive six months of IPT, followed by BCG immunization. Breastfeeding may be safely continued during this period.

4.2.2 Diagnosis of tuberculosis in children

The diagnosis of TB in children relies on a careful and thorough assessment of all the evidence derived from an accurate history, clinical examination and relevant investigations, e.g. TST, CXR and sputum smear microscopy. Although bacteriological confirmation of TB is not always feasible, it should be sought whenever possible, e.g. by sputum smear microscopy for children with suspected pulmonary TB who are old enough to produce a sputum sample. A trial of treatment with anti-TB medication is not recommended as a method for diagnosing TB in children. The decision to treat a child should be carefully considered; once such a decision is made, the child should be treated

with a full course of therapy. Standard international case definitions apply to adults and children. In most immunocompetent children, TB presents with symptoms of a chronic disease after they have been in contact with an infectious source case. Box 4.1 outlines the key risk factors for TB in children.

BOX 4.1

KEY RISK FACTORS FOR TUBERCULOSIS

- Household contact of a newly diagnosed smear-positive case
- Aged less than 5 years
- HIV infection
- Severe malnutrition

Box 4.2 shows the key features suggestive of TB in children. Infection with *M. tuberculosis* can usually be demonstrated by a TST (although less reliably in the presence of HIV infection). The clinical presentation in infants may be more acute, resembling acute severe pneumonia, and should be suspected when there is a poor response to antibiotics. In such situations, there is often an identifiable source case, usually the mother.

BOX 4.2

KEY FEATURES SUGGESTIVE OF TUBERCULOSIS

A diagnosis of tuberculosis is strongly suggested in the presence of three or more of the following:

- chronic symptoms suggestive of tuberculosis
- physical signs highly suggestive of tuberculosis
- a positive tuberculin skin test
- chest X-ray suggestive of TB.

Existing diagnostic tests for TB in children have shortcomings, and the full range of tests (including bacteriological culture and TST) is often not available in settings where the disease is diagnosed in the vast majority of cases.

In some countries, score charts are used for the diagnosis of TB in children. These charts have rarely been evaluated or validated against a “gold standard” and should therefore be used as screening tools and not as the means of making a firm diagnosis. Score charts perform particularly poorly in children suspected of pulmonary TB and in children who are also HIV-infected.

Box 4.3 summarizes WHO’s recommended approach for the diagnosis of TB in children. Children are equally susceptible to drug-resistant and to drug-susceptible TB. Drug-resistant TB is a laboratory diagnosis. However, drug-resistant TB should be suspected if any of the features below are present.

BOX 4.3

RECOMMENDED APPROACH FOR DIAGNOSIS OF TUBERCULOSIS IN CHILDREN

1. Careful history (including history of TB contact and symptoms consistent with TB)
2. Clinical examination (including growth assessment)
3. Tuberculin skin testing
4. Bacteriological confirmation whenever possible
5. Investigations relevant for suspected pulmonary or extrapulmonary TB
6. HIV testing (in areas of high HIV prevalence)

1. *Features in the source case suggestive of drug-resistant TB*

   - contact with a known case of drug-resistant TB;
   - remains sputum smear-positive after three months of treatment;
   - history of previously treated TB;
   - history of treatment interruption.

2. *Features of a child suspected of having drug-resistant TB*

   - contact with a known case of drug-resistant TB;
   - not responding to the anti-TB regimen;
   - recurrence of TB after adherence to treatment.

4.2.3 Treatment of tuberculosis in children

Chapter 2 details the drug doses recommended by WHO for TB in children.

Children usually have paucibacillary pulmonary disease (low organism numbers), as cavitating disease is relatively rare (about 6% of cases or fewer) in those aged under 13 years (the majority of the organisms in adult-type disease are found in the cavities). In contrast, extrapulmonary TB occurs more commonly in children than in adults. Severe and disseminated TB (e.g. TB meningitis and miliary TB) occur especially in young children (aged under 3 years). Both the bacillary load and the type of disease may influence the effectiveness of anti-TB regimens. Treatment outcomes in children are generally good, even in young and immunocompromised children who are at higher risk of disease progression and disseminated disease, provided that treatment starts promptly. There is a low risk of adverse events associated with use of the recommended regimens.

The recommended anti-TB regimens for each diagnostic category are generally the same for children as for adults (see Table 2.2). New cases fall within Category I (new smear-positive pulmonary TB; new smear-negative pulmonary TB with extensive parenchymal involvement; severe forms of extrapulmonary TB; severe concomitant HIV disease) or Category III (new smear-negative pulmonary TB other than in Category I; less severe forms of extrapulmonary TB).

Most children with TB have uncomplicated (smear-negative) pulmonary or intrathoracic TB or non-severe forms of extrapulmonary TB. They therefore come within WHO TB

diagnostic Category III: the recommended treatment regimen is 2HRZ/4HR (or 2HRZ/6HE). A minority of children have smear-positive pulmonary TB, extensive pulmonary involvement or severe forms of extrapulmonary TB (e.g. abdominal or TB of the bones or joints). They therefore come within diagnostic Category I: the recommended treatment regimen is 2HRZE/4HR (or 2HRZE/6HE). Children with TB meningitis and miliary TB require special consideration (see WHO *Guidance for national tuberculosis programmes on the management of tuberculosis in children*). Previously treated cases fall under diagnostic Category II (previously treated smear-positive pulmonary TB) or Category IV (chronic cases and MDR-TB).

Use of corticosteroids. Corticosteroids may be used for the management of some complicated forms of TB, e.g. TB meningitis, complications of airway obstruction by TB lymph glands and pericardial TB. In cases of advanced TB meningitis, corticosteroids have been shown to improve survival and decrease morbidity. Corticosteroids may be useful in some cases of immune reconstitution.

Treatment support. Children, their parents and other family members, and other caregivers should be educated about TB and the importance of completing treatment. Treatment is usually administered by the child's mother or other caregiver. Support from the child's parents and immediate family is vital to ensure a satisfactory treatment outcome. Often, a health-care worker can observe and record the treatment, but if this arrangement is not convenient for the family, a trained community member (preferably someone other than the child's parent or immediate family) can undertake this

responsibility. All children should receive treatment free of charge, whether the child is smear-positive at diagnosis or not. FDCs should be used whenever possible to improve simplicity of and adherence to treatment. Patient treatment cards are recommended for documenting treatment adherence.

Hospital care. Children with severe forms of TB should be hospitalized for intensive management where possible. Conditions that merit hospitalization include: (i) TB meningitis and miliary TB, preferably for at least the first two months; (ii) respiratory distress; (iii) spinal TB; and (iv) severe adverse events, such as clinical signs of hepatotoxicity (e.g. jaundice). If it is not possible to ensure good adherence and treatment outcome on an outpatient basis, some children may require hospitalization for social or logistic reasons.

HIV-infected children. Most current international guidelines recommend that TB in children infected with HIV should be treated with a six-month regimen, as for children who are not infected with HIV. Where possible, HIV-infected children should be treated with rifampicin for the entire duration of treatment, as higher relapse rates among HIV-infected adults have been found when ethambutol is used in the continuation phase. Most children with TB, including those who are HIV-infected, have a good response to the six-month regimen. Possible causes of failure, such as non-compliance with therapy, poor drug absorption, drug resistance and alternative diagnoses, should be investigated in children who are not improving on anti-TB treatment.

All children with TB and HIV coinfection should be evaluated to determine whether ART is indicated during the course of treatment for TB. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. Given the complexity of co-administration of anti-TB treatment and ART, consultation with an expert in this area is recommended before initiation of concurrent treatment for TB and HIV infection, regardless of which disease appeared first. However, initiation of treatment for TB should not be delayed. Children with TB and HIV coinfection should also receive co-trimoxazole as prophylaxis for other infections.

In HIV-infected children with confirmed or presumptive TB disease, initiation of anti-TB treatment is the priority; however, the optimal timing for ART initiation is not known. The decision on when to start ART after starting anti-TB treatment involves a balance between the child's age, pill burden, potential drug interactions, overlapping toxicities and possible IRIS versus the risk of further progression of immune suppression with its associated increase in mortality and morbidity. Many clinicians start ART 2–8 weeks after starting anti-TB treatment.

4.2.4 Recording and reporting

Children with TB should always be included in the routine NTP recording and reporting system (see Chapter 3). It is crucial to notify the NTP of all identified TB cases in children, register them for treatment and record their treatment outcome. At the end of the treatment course for each child with TB, the district TB officer should record the standard outcome in the district TB register. Four of the standard outcomes are applicable to

children with smear-negative pulmonary or extrapulmonary TB: treatment completion, default, death and transfer out.

Recording and reporting two age groups for children (0–4 years and 5–14 years) in the TB registers is useful for drug procurement (in child-friendly formulations for young children) and to monitor trends of case-finding and treatment outcomes. Evaluation of treatment outcome by cohort analysis in children is a valuable indicator of the quality of programmes for child TB patients. For TB/HIV indicators in children, see Chapter 13.

4.3 Main activities to be carried out by the national TB control programme for implementation of interventions to prevent and manage tuberculosis in children

Implementation by the NTP of interventions to prevent and manage childhood TB requires the activities listed below.

1. Preparations:

- advocate to health authorities for mainstreaming of "childhood TB interventions" as part of routine NTP activities, in collaboration with the maternal and child health programme;
- conduct a situation analysis of the extent to which childhood TB interventions are mainstreamed as part of routine NTP activities, of currently available data on prevention, case finding and treatment outcome, and of resources available for implementation of childhood TB interventions;
- adapt NTP guidelines to reflect childhood TB interventions;

- adapt maternal and child health guidelines to reflect childhood TB policies;
- engage with key community stakeholders (academics, activists, etc.) to develop appropriate information, education and communication (IEC) material;
- in settings with high HIV prevalence, ensure effective linkages with HIV control services.

2. Facilitate meetings with relevant health and other authorities at national, regional or provincial and district level, to ensure engagement of all health providers (government, nongovernmental organizations, private sector, religious and charity organizations, etc.)

3. Training to implement childhood TB interventions:

- develop and produce training material for health staff based on national guidelines;
- develop and produce training material for community participants (e.g. those involved in contact tracing and case-finding, and in promoting and encouraging adherence as “treatment supporters”);
- sensitize health staff and relevant community members regarding the nature and extent of the problem of childhood TB, and motivate them to share responsibility for contact tracing, case-finding and treatment support.

4. Delivery of childhood TB interventions as part of routine NTP activities

- assess drug procurement system for effectiveness in ensuring availability of quality-assured formulations of anti-TB drugs for children (and consider obtaining these drugs through the GDF);

- monitor results of contact tracing, case-finding and treatment support;
- check how effectively the routine NTP recording and reporting system is capturing the data on case-finding and treatment outcomes;
- evaluate how effectively the full range of health providers is mobilized to contribute to making high-quality childhood TB interventions universally accessible;
- assess effectiveness of the system of procurement of tuberculin.

5. Advocacy, communications and social mobilization (ACSM) activities

- incorporate messages about childhood TB in ACSM activities for health promotion;
- advocate for commitment and funds to ensure universal access to high-quality childhood TB interventions as part of routine NTP activities.

WHO guidelines

Guidance for national tuberculosis programmes on the management of tuberculosis in children. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.371; WHO/FCH/CAH/2006.7).

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Chapter 5 Contact investigation

A review of contact investigations carried out in low-income and middle-income countries showed that 4.5% of identified household contacts of new pulmonary TB cases had TB at the time of the evaluation, of whom 2.3% had bacteriologically-confirmed TB. Among contacts aged under 5 years, 8.5% were found to have TB. More than 50% of household contacts had latent TB infection (LTBI). WHO and the International Union Against Tuberculosis and Lung Disease (the Union) recommend targeting children aged under 5 years for contact investigation and treatment of LTBI in low-income countries where full implementation of contact investigations may not be feasible. The findings indicate the need for policies to address LTBI among close contacts in settings of high TB incidence. In low-incidence settings approaching the elimination phase, contact investigation plays a significant role in TB control (see Annex).

5.1 Standards for contact investigation

The implementation of TB contact investigation activities by the NTP should use clear definitions of the TB index case and contacts, procedures to be used in evaluating contacts, policies for treating LTBI and monitoring of the results of contact investigations. These definitions are not well standardized at the global level and vary among countries/areas and even within countries. Decisions about contact investigation and treatment of LTBI should be based on the burden of TB in the country and the resources available.

5.2 Definitions for contact investigation

Before undertaking contact investigations, precise definitions for the index case and for the contacts need to be established.

5.2.1 Index case

All smear-positive pulmonary TB cases should be considered as index cases; their contacts should be evaluated for TB. All children with TB should be considered as index cases; the purpose of contact investigation is to identify the source of TB transmission. Some countries may use broader definitions, for example including as index cases other forms of TB such as smear-negative pulmonary TB cases, or any form of pulmonary TB irrespective of its bacteriological status.

5.2.2 Contacts

TB contacts should be clearly defined in terms of the type of contact, and the closeness and duration of exposure to the index case. In many developing countries, a TB contact is defined as any household member at the moment of the identification of the index case. All children in the household, especially those aged under 5 years, should be assessed for TB. High priority should also be given to contacts who have HIV infection and those with other underlying risk factors for TB. The definition of contacts may be extended to include individuals in congregate settings (e.g. the workplace, schools, social gatherings, prisons, hospitals, other health facilities) if prolonged contact with an index case has taken place.

5.3 Process of contact investigation

The index case should be interviewed as soon as possible after diagnosis to identify contacts. The interview should, as a first priority, focus on the household, but the questions should cover other environments, as mentioned above. Ideally, the interview should be conducted by a person familiar with the culture and the setting. Wherever possible, a home visit should be made to obtain a clearer understanding of the patient's circumstances and to confirm the results of the interview.

All identified prioritized contacts of the index case should be instructed to come to the health facility for evaluation. The identified contacts should be listed; if they do not appear for evaluation, a home (or other setting) visit should be made. As a priority, every effort should be made to assess children and people living with HIV/AIDS or those with other conditions and situations associated with an increased risk of TB. After listing the contacts, the results of their assessment should be recorded.

The procedure for screening TB contacts should be clearly defined. The evaluation may be limited to determining whether the contact has symptoms that may suggest TB. As a minimum, all adolescent and adult TB contacts should be asked whether they have a persisting cough (>2 weeks). Sputum smear examinations should be carried out on those with a persistent cough. All children and PLHIV should be more thoroughly assessed for TB, including of extrapulmonary sites.

5.4 Provision of treatment

Four important considerations should be taken into account when providing treatment.

(i) Any contact identified as having active TB should be registered and treated in line with the NTP policy.

(ii) Children aged under 5 years who are close contacts and who do not have evidence of TB should be systematically treated with isoniazid chemoprophylaxis: 5 mg/kg daily for six months.

(iii) Children aged 5 years and above who are in good health do not require chemoprophylaxis but should be followed up on a clinical basis.

(iv) PLHIV who are close contacts of an infectious index case and who do not have evidence of TB should be treated with isoniazid: 300 mg/day for 6–9 months.

5.5 Follow-up of treatment

All patients receiving isoniazid preventive therapy (IPT) should be seen at regular intervals at least early in the course of treatment to determine whether any adverse effects of isoniazid occur and to encourage adherence. After completing treatment, patients should be asked to seek care if a cough or other possible symptoms of TB develop; there is no need for further follow-up. Likewise, contacts with no evidence of TB should be asked to visit a health facility if a persistent cough or other symptoms develop in the following weeks or months.

5.6 Monitoring

The implementation of TB contact investigation activities requires a monitoring and evaluation system to provide information on (i) the process of TB contact investigation, (ii) the yield of TB contact screening and (iii) the activities and monitoring of IPT. A model of register for contacts is proposed in the WHO recording and reporting system.

5.7 Tuberculosis and international air travel

Transmission of *M. tuberculosis* infection may occasionally occur in passengers seated in close proximity to an infectious TB patient on board an aircraft during prolonged flights (flights exceeding 8 hours). In no case has active TB been reported subsequently among such contacts. The risk of infection during prolonged air travel is estimated to be similar to (or less than) the risk in other congregate settings. Following an incident involving possible exposure to an infectious TB case on a long-haul flight, contact investigations are recommended for the passengers seated in the same row and in the two rows in front and the two rows behind the index case (i.e. five rows), and air crew working in the same cabin area. WHO has published guidelines on procedures and responsibilities for the prevention and control of TB associated with air travel (see below).

WHO guidelines

Guidance for national tuberculosis programmes on the management of tuberculosis in children. Geneva, World Health Organization, 2006 (WHO/HTM/TB/2006.371).

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Chapter 6 Infection control in health-care settings

Following the introduction of short-course chemotherapy in the 1980s, measures to improve infection control in health-care settings received relatively low priority. Given the rapid sterilizing effect of rifampicin, the isolation of infectious TB patients from other hospital patients and from the community was no longer considered important. As a result, TB isolation wards were discontinued, and measures such as cough hygiene and wearing of surgical masks by infectious patients were no longer encouraged. The risk of infection for health workers was not thought to require any specific policy or preventive measures except for laboratory staff dealing with culture and DST of *M. tuberculosis*.

The increasing importance of drug-resistant TB, as well as the impact of HIV infection, has led to a reappraisal of the importance of infection control in health-care and other congregate settings. The presence of many HIV-infected and immunocompromised patients plus health-care workers in hospitals together with the absence of appropriate infection control policy and practice creates a favourable environment for transmission and spread of TB among hospital patients, hospital workers and the community. There is therefore an urgent need to refocus attention on TB infection control, particularly in high-risk settings.

6.1 Risk of transmission of tuberculosis in health-care settings

Health-care workers are at much higher risk of TB infection and disease compared with the general population. In health-care settings, other non-medical staff may also be at risk through contact with infectious sources. Measures to control infection are needed in all

settings where there is a significant risk of transmission of TB infection. These settings include general health facilities where patients with cough and in whom pulmonary TB has been diagnosed are in close contact with health staff and others in a crowded and poorly ventilated environment.

Waiting rooms (or corridors) where patients and accompanying people, including children, wait to receive medical care are often areas of particular risk. In hospitals, the risk of transmission is relatively high, especially in pulmonary disease wards. The risk of spread increases when the prevalence of HIV in the contacts (staff and other patients) is high. Laboratories, particularly those carrying out *M. tuberculosis* culture procedures, are also high-risk areas. Other high-risk settings include institutions such as jails, prisons and detention centres, and drug rehabilitation centres. Other situations, such as enclosed environments during prolonged travel, may require special attention.

There are specific strategies to address infection control, but the main infection control measure is the proper organization and implementation of case detection procedures. Patients receiving adequate treatment are rapidly rendered non-infectious.

6.2 Infection control strategies

The three levels of TB infection control are workplace and administrative (managerial) control measures, environmental control measures and personal protective equipment (respiratory protection). Each level operates at a different point in the transmission process:

- workplace and administrative control measures reduce the exposure of staff and patients;
- environmental control measures reduce the concentration of infectious droplet nuclei;
- personal protective equipment (respiratory protection) protects staff in specific settings where the concentration of droplet nuclei cannot be adequately reduced by administrative and environmental control measures.

6.2.1 Workplace and administrative control measures

Workplace and administrative control measures have the greatest impact on preventing TB transmission. They serve as the first line of defence for preventing the spread of TB in health-care settings. The goals are (i) to prevent TB exposure of staff and patients and (ii) to reduce the spread of infection by ensuring rapid and recommended diagnostic investigation and treatment for patients and staff suspected or known to have TB.

The five components of good workplace and administrative control are:

- an infection control plan;
- administrative support for procedures contained in the plan, including quality assurance;
- training of health-care and other staff;
- education of patients and increasing community awareness;
- coordination and communication with the TB control programme.

Each facility should have a written TB infection control plan with a protocol for the prompt recognition, separation, provision of services, investigation for TB and referral of patients with suspected or confirmed TB disease. A designated infection control officer is responsible for overseeing the implementation of infection control measures and providing infection control training for health-care and other staff who may be exposed to TB infection.

All staff working in a facility should understand the importance of infection control policies and their role in implementing them. As part of training, each health-care worker and staff member, including any lay workers, should receive job category-specific instruction. Training should be conducted before initial assignment, and continuing education should be provided to all employees and volunteers annually.

Reminders that health-care workers and other staff can develop TB, regardless of previous infection status or BCG vaccination, should be given as part of annual retraining on infection control. Staff should be investigated for TB free of charge if they have a cough for two weeks or longer. The infection control plan should list designated staff members to be contacted to initiate confidential TB investigations.

Patients should receive instruction on how to protect others from exposure to TB by simple cough hygiene measures.

6.2.2 Environmental control measures

Environmental controls are the second line of defence for preventing the spread of TB in health-care settings. It is important to recognize that if workplace or administrative controls are inadequate, environmental controls will not eliminate the risk. Many environmental control measures are technically complex and expensive, and therefore only practical for referral hospitals.

Environmental controls include:

- ventilation (natural and mechanical)
- filtration
- ultraviolet germicidal irradiation.

Ventilation. Controlled natural ventilation considerably reduces the risk of spreading *M. tuberculosis*. When fresh air enters a room, it dilutes the concentration of particles in room air, such as droplet nuclei containing *M. tuberculosis*. Natural ventilation relies on open doors and windows to bring in air from the outside; controlled natural ventilation includes checks to ensure that doors and windows are maintained in an open position that enhances ventilation. Fans may also assist in distributing the air. However, the use of ceiling fans is only justified if there is free air flow out from the room through open windows. Designing waiting areas and examination rooms to maximize natural ventilation can significantly reduce the spread of TB. In warm climates, open-air shelters with a roof to protect patients from sun and rain are appropriate.

Negative pressure ventilation is another method used to prevent contaminated air from flowing out of the room into adjacent areas in laboratory or health-care facilities, by maintaining an air pressure difference between the two areas. Air is drawn into the room from adjacent areas and exhausted directly to the outside, removing and diluting any infectious particles. This may be the method of choice in some settings, depending on factors including climatic conditions and available resources. The necessary equipment requires continued maintenance and the air exchange rate may be less than that achieved by well-designed natural ventilation.

When patients provide sputum smear specimens for TB diagnosis, they should do so outside, in the open air away from other people. When this is not possible because of climatic constraints, it should be done in an adequately ventilated booth and not in small rooms such as toilets or other enclosed areas.

Filtration. In small rooms with a limited number of patients or in other small, enclosed areas, room air cleaners with high efficiency particulate air (HEPA) filters may be a useful alternative to mechanical ventilation requiring structural changes. Room air cleaners with HEPA filters may be free-standing or may be permanently attached to floors or ceilings to minimize tampering. Correct maintenance of the filter is essential.

Ultraviolet germicidal irradiation. *M. tuberculosis* is killed if the organisms are exposed to sufficient ultraviolet germicidal irradiation (UVGI). However, effectiveness depends on close contact with the UV light source and may be limited if humidity is high (over 60%) and

where dust levels are high. UV lights should be directed to the ceiling, associated with adequate air flow and regularly maintained. The major concerns about inadequately installed and maintained UVGI have been adverse reactions, such as acute and chronic skin and eye changes resulting from overexposure. For these reasons, and because of inability to assess its effectiveness in field conditions, UVGI is not generally recommended as a method to disinfect room air in patient wards.

6.2.3 Personal protective equipment (respiratory protection)

Personal respiratory protection involves training in the selection and use of respirators. Respirators should not be relied upon to protect health care workers from inhaling *M. tuberculosis* in the absence of standard workplace and environmental controls. They are expensive, require specialized equipment to ensure proper fit and are often unavailable in resource-limited settings. Their use should be restricted to specific high-risk areas in hospitals and referral centres, such as rooms where spirometry or bronchoscopy are performed or specialized treatment centres for patients with MDR-TB. If a respirator is needed, a USA-certified N95 (or greater) or EU-certified FFP2 (or greater) respirator should be used.

Respirators should be distinguished from face masks, such as surgical masks made of cloth or paper. Use of face masks is not generally recommended for health-care staff because they do not protect against TB transmission by aerosol.

However, the use of face masks in high-risk settings for drug resistant-TB is recommended for patients to reduce the risk of droplet nuclei generation and spread, particularly in high-prevalence HIV settings where many health-care workers may be HIV-infected. Respiratory protection may be used as an interim measure while selected administrative and/or environmental control measures are awaiting implementation.

WHO guidelines

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Chapter 7 Isoniazid preventive therapy

Preventive therapy, also known as chemoprophylaxis, with isoniazid reduces the risk of (i) a first episode of TB occurring in people exposed to infection or with latent infection and (ii) a recurrent episode of TB. Although all people with latent TB infection who take isoniazid benefit, the greatest reduction in infection is observed in HIV-negative patients and in TST- and HIV-positive individuals.

WHO recommends isoniazid taken at a daily dose of 5 mg/kg (maximum 300 mg) for at least six months, and ideally for nine months. Shorter rifampicin-containing regimens have shown similar efficacy compared with 6–9 months of isoniazid monotherapy, but rifampicin-containing regimens are more likely to be discontinued because of adverse effects. Increased rates of hepatotoxicity and death in HIV-uninfected individuals have been reported for regimens containing rifampicin and pyrazinamide. However, this risk appears to be limited to HIV-uninfected individuals, as a rigorous re-analysis of a large trial of rifampicin and pyrazinamide in HIV-infected patients confirmed an absence of serious toxicity.

Preventive therapy has been used mainly for its beneficial effect in the individual. At a population level, mathematical modelling of community-wide preventive therapy in settings with a high burden of both HIV and TB suggests that this strategy may contribute to a reduction in the incidence of TB.

The impact of preventive therapy programmes on the emergence of drug resistance is not yet known. Limited findings do not exclude an increased risk of isoniazid-resistant TB after IPT.

The main groups for preventive therapy under programmatic conditions are those at most risk of progressing to TB disease. These are (i) PLHIV, (ii) infants and children who are contacts of TB patients and (iii) recent TST converters, since the risk of developing active TB is increased in the first few years.

7.1 Isoniazid preventive therapy in children

See Chapter 4.

7.2 Isoniazid preventive therapy in recent TST converters

Treatment with isoniazid of TST-positive individuals living in settings with high prevalence of TB is highly efficacious in reducing the risk of developing active TB. Preventive therapy is therefore recommended for TST-positive individuals who do not have active TB.

TST may not identify recently infected contacts, especially children, and may not be positive in people with *M. tuberculosis* and HIV coinfection because of reduced immune responsiveness. TST may also be negative in approximately 25% of HIV-negative people with active TB.

7.3 Isoniazid preventive therapy in people living with HIV

The risk of TB in individuals infected with both *M. tuberculosis* and HIV is much higher than for those without HIV infection, at 5–10% risk per year and 5–10% lifetime risk respectively. Treatment with isoniazid of individuals who are both TST- and HIV-positive, living in settings with high prevalence of TB, reduces the risk of developing active TB by around 60% (i.e. to around 40% of what it would have been without the treatment). WHO therefore recommends that information about IPT should be made available to all PLHIV and that IPT should be offered, as part of the package of care, to all TST-positive HIV-infected individuals in whom active TB has been safely excluded.

In situations where TST cannot be performed, treatment of HIV-positive individuals with isoniazid reduces the risk of developing active TB by around 40% (i.e. to around 60% of what it would have been without the treatment). If TST testing is not available, the following individuals should be considered for preventive therapy if they are infected with HIV:

- people living in populations with a high prevalence of *M. tuberculosis* infection (estimated to be >30%);
- health-care workers;
- household contacts of TB patients;
- prisoners;
- miners;
- other selected groups at high risk of acquiring or transmitting TB.

TB and HIV control programmes should collaborate to ensure provision of IPT as part of the package of care for PLHIV when active TB has been excluded, and information about IPT should be made available to all PLHIV. Since PLHIV are usually in contact with health-care services, there are opportunities to provide IPT and encourage adherence.

All people attending HIV counselling and testing should be asked whether they have a cough and other symptoms such as fever or weight loss; those who do should be screened for TB. Those found to have TB should be registered and treated by the TB control programme. CXR is recommended to exclude active TB before considering preventive therapy. (However, exclusion of active TB may be more difficult in this group as many HIV-positive patients are smear-negative and radiographic findings may be less specific.) Screening based solely on symptoms has been found adequate to exclude active TB among asymptomatic HIV-positive patients in trial settings. The efficacy of using symptom-based screening alone to exclude active TB in programmatic settings needs to be validated.

In populations with a high prevalence of TB, the duration of benefit following completion of a full six-month course of IPT is limited (up to 2.5 years). This is probably the result of continued exposure to *M. tuberculosis* infection.

The use of preventive therapy in combination with ART for PLHIV may be beneficial but has not been fully evaluated. Preventive therapy given after a full course of anti-TB treatment has reduced the risk of recurrent TB in PLHIV in several settings, but did not

prolong survival. However, the risks resulting from not using IPT should be taken into account (infection control, increased morbidity, transmission, etc.).

7.4 Preventive therapy in pregnancy

WHO recommends treatment of active TB during pregnancy but has not developed recommendations on preventive therapy during pregnancy (see Chapter 2). The use of IPT when clinical and laboratory monitoring cannot be ensured is controversial because of reports of isoniazid-related hepatotoxicity in pregnant and postpartum patients.

WHO guidelines

Chronic HIV care with ARV therapy and prevention: interim guidelines for health workers at health centre or district hospital outpatient clinic. Geneva, World Health Organization, 2006 (available at: http://www.who.int/3by5/publications/documents/chronCareModGenDraftRev1.pdf; accessed February 2008).

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Chapter 8 BCG vaccination

Coverage with BCG vaccine reaches >80% of neonates and infants in countries where it is part of the national childhood immunization programme. BCG vaccine has documented protective efficacy against TB meningitis and miliary disseminated disease in children (86% on average). It does not prevent primary infection and, more importantly, does not prevent reactivation of latent pulmonary infection, the principal source of bacillary spread in the community. The impact of BCG vaccination on transmission of *M. tuberculosis* is therefore limited.

WHO recommendations on the use of BCG vaccine

- In countries with a high burden of TB, a single dose of BCG vaccine should be given to all infants as soon as possible after birth. Since severe adverse effects of BCG vaccination are extremely rare, all healthy neonates should be BCG-vaccinated, even in areas endemic for HIV.
- BCG vaccination should ***not*** be given to (i) infants and children with AIDS, (ii) infants and children known to be HIV-infected or (iii) children known to have other immunodeficiencies. .
- In situations where infants have been exposed to smear-positive pulmonary TB shortly after birth, BCG vaccination should be delayed until completion of six months of IPT.

- Vaccination of health staff, and particularly laboratory workers, is an option in high-risk environments (in particular if staff are in close contact with cases of drug-resistant TB).
- There is no evidence that revaccination increases protection, and revaccination is not recommended.
- Countries with a low burden of TB may choose to limit BCG vaccination to neonates and infants of recognized high-risk groups for the disease or of TST-negative older children. In some low-burden populations,[1] BCG vaccination has been replaced by intensified case detection and supervised early treatment.

Until an improved anti-TB vaccine becomes available, efforts to control the spread of the disease will continue to rely on currently available tools, namely early diagnosis and treatment, appropriate preventive treatment, and other public health and infection control measures.

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[1] A low-burden population is defined as a population with (i) an annual notification rate of smear-positive pulmonary TB cases below 5 per 100 000; or an average annual notification rate of tuberculous meningitis in children aged <5 years below 1 per 10 million population during the previous five years; or an average annual risk of tuberculous infection below 0.1%.

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Chapter 9 Prevention through addressing risk factors

Changes in exposure to various risk factors may significantly influence trends in the incidence of TB (see Introduction – Epidemiology of tuberculosis). Reducing the level of exposure of the population to risk factors including HIV, smoking, diabetes, malnutrition and crowding is mainly the responsibility of other public health programmes as well as stakeholders outside the health sector. The capacity and mandate of NTPs to help reduce the prevalence of these risk factors in the general population are limited. Nevertheless, NTPs have an important role to play in advocating the need to address such risk factors and in supporting implementation of other public health programmes as part of integrated service delivery in primary health care. HIV/AIDS is discussed in Chapter 13. Other selected risk factors with potential population-level importance for TB control are outlined below. The evidence base for several of these risk factors needs to be strengthened.

9.1 Smoking

Both active and passive smoking increase (i) susceptibility to TB infection, (ii) progression to active TB disease and (iii) the risk of adverse anti-TB treatment outcomes. Systematic reviews suggest that the risk of TB disease among smokers is increased two- to threefold compared with people who have never smoked. There is insufficient evidence to support an association of smoking and patient delay, default, slower smear conversion or risk of acquired drug resistance. Weighted smoking prevalence across countries with a high TB burden was about 18% in 2004–2005, with much higher prevalence among men than among women in most countries. The prevalence of smoking is increasing in developing countries.

Tobacco control and smoking cessation among people with TB can therefore play an important role in limiting the burden of TB. NTPs should support activities to control use of tobacco at national and local levels. Smoking cessation could be a part of the package of services delivered under PAL (see Chapter 23).

9.2 Malnutrition

Malnutrition is common in most countries with a high TB burden. The weighted prevalence of undernutrition, as defined by the Food and Agriculture Organization of the United Nations, across the high TB burden countries is almost 20%. Malnutrition may be linked to increased risk for TB disease through immune deficiency caused by deficiencies in protein, energy and/or micronutrients (vitamins and minerals). Estimates of relative risk for TB disease differ considerably for different types of malnutrition and in different populations. However, the historical importance of improved nutrition to help control TB in many countries that now have a low TB burden is well established. NTPs should therefore advocate for improved nutritional status in the population, as part of a long-term TB control and elimination strategy.

NTPs may consider nutritional support to TB patients as a part of the package of clinical care for patients, who are often malnourished at the time of diagnosis. This would benefit patients and contribute to the implementation of broader nutritional programmes. However, it is unclear whether nutritional support improves treatment outcomes for TB patients. Since treatment success rates exceeding 85% can be achieved without nutritional support, this intervention may not prove to be essential to reach treatment success targets.

The evidence base concerning the added value of different types of nutritional support for TB patients needs to be strengthened.

9.3 Diabetes mellitus

Estimates of the relative risk for developing TB (all types) among people with diabetes (type I or II) compared with control groups range between 1.5 and 8. Diabetes prevalence is increasing globally, including in many countries where the burden of TB is high. The implication for the TB burden of changing diabetes prevalence is unclear. Future TB control strategies may need to include explicit efforts to support public health programmes aimed at reducing diabetes prevalence and improving management of diabetes.

9.4 Crowding

Crowding is a classical TB risk factor. Household occupation density, ventilation and humidity influence the risk of exposure to infectious droplets. The precise increase in risk associated with different levels of crowding is not well established. It is clear, however, that improved living conditions in private dwellings and in various residential institutions can have an important impact on the transmission of TB.

9.5 Indoor air pollution

Indoor air pollution caused by indoor burning of solid fuels without proper ventilation is a common phenomenon in most poor countries. More than 70% of households in high TB burden countries are exposed to this health hazard. A limited body of evidence suggests that

indoor air pollution may increase the risk of TB. If a causal link is confirmed, the implications at the population level will be important given the high prevalence of exposure. NTPs might advocate for further research on this topic.

9.6 Alcohol abuse and dependency

The increased risk of TB disease among people who abuse alcohol has been shown in many studies. Analytical epidemiological studies that have controlled for important confounding factors have reported relative risk of TB disease ranging between 2 and 8 for people with very high alcohol consumption or a diagnosis of alcohol abuse or alcohol dependence. This risk increase might be explained by specific social mixing patterns and living conditions for people abusing alcohol leading to increased risk of infection as well as by compromised immunity linked to toxic effects of alcohol or to medical conditions caused by alcohol abuse. A definite causal link between alcohol abuse and TB disease has not yet been established.

9.7 Silicosis and other rare chronic conditions

Silicosis, and a wide range of other chronic diseases, malignancies, systemic illnesses and immunosuppressant treatments, increases the risk of TB disease dramatically. Prevalence of silicosis is high in certain population groups where employment in the mining industry is common. Most of the other risk factors are probably of limited importance at a population level.

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Part II Programmatic management of tuberculosis

The NTP is one of the components of the national health system. It is responsible for ensuring that the entire health system carries out the actions necessary to reduce mortality and morbidity from TB and interrupt transmission of the disease. This requires linkages and collaboration outside the ministry of health, since many health-care facilities are governed by other ministries, such as those for justice, defence, labour, education, social welfare and transport. The NTP is also responsible for communicating to decision-makers outside the health sector the need to address the socioeconomic and environmental determinants of TB in order to ensure long-term control and elimination of the disease (see Chapter 9).

The NTP is responsible for setting policy standards, developing programme guidelines and training materials, ensuring that sufficient financial and human resources are available, and monitoring the process and results of programme implementation. In an integrated system, it is responsible for ensuring that TB-related services are provided properly through general health services. For effective TB services to reach all sections of the population, the NTP should work in close collaboration with communities and with all relevant public as well as private health-care providers. Chapter 10 outlines the normal structure, organization and functions of an NTP.

Chapter 10 Managerial structure

10.1 Organization of national tuberculosis control programmes

Some of the key elements of effective TB control programme management are:

- a central unit in the ministry of health, to ensure political, technical and operational support, provide stewardship, generate resources and oversee programme management;
- clearly identified and accountable district/BMU TB coordinators;
- strategic and technical documents and plans: a programme manual, including technical and operational guidelines, NTP medium-term strategic plan and annual operational plan, and economic analysis to make best use of resources;
- a human resources development programme and plan, to cover all aspects of national policy for TB control;
- a recording and reporting system, to provide data for monitoring and evaluation;
- a training programme covering all aspects of the national policy for TB control;
- a nationwide functional quality assurance system, to promote high-quality standards in all facilities involved in TB services;
- a network of quality-assured laboratory services for bacteriological diagnosis of TB;
- a service network for TB care diagnosis and treatment, involving public and private primary health-care providers and the other levels of the health-care system;
- a procurement and distribution system that ensures a regular supply of high-quality drugs and diagnostic materials;

- a monitoring and evaluation system, including a recording and reporting system, a supervision programme and the provision of technical support to peripheral levels;
- organized supervision and technical support;
- national committees or partnerships to promote TB care, including collaboration with other programmes such as the national HIV control programme;
- a system of advocacy, communication and social mobilization;
- planning, including economic analysis to make best use of resources;
- operational research activities.

The direct responsibilities and resources of the NTP will vary according to the political structure and health system of the country as well as the national TB burden.

- The development of guidelines and training materials with involvement of technical experts (academia, clinical institutions, institutions that provide training) is usually a direct responsibility of the NTP.

- Bacteriology services are usually a part of, and the responsibility of, the general laboratory services network. NTP input may vary from coordination only to ensuring services by providing support, planning, supervision and monitoring.

- Drug supplies may be financed, procured and distributed by the NTP, or its involvement may be limited to planning and monitoring, with procurement and distribution ensured through the essential drug programme of the ministry of health.

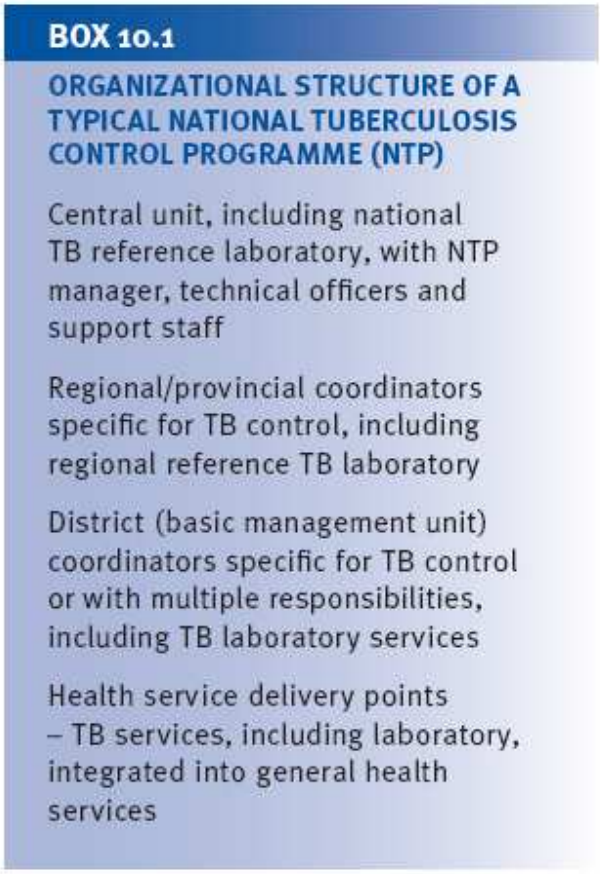
Service delivery should be integrated at the peripheral level of the health services. The need for specialized institutions and professionals (second and third level of care) will vary according to the burden of disease. To ensure appropriate service delivery at the peripheral level, the NTP usually has the following organizational structure (Box 10.1):

- *Central level*. The central unit in some NTPs has direct access to and pays the salaries of health workers at the peripheral-level health facilities and district hospitals that provide diagnosis and treatment of TB. The central unit coordinates support at all levels for the service delivery at the peripheral level. Its functions are summarized in section 10.2 below.

- *Regional/provincial level*. In many countries, service delivery is coordinated and facilitated from regional- or provincial-level settings. In many large countries, the NTP has a full-time TB coordinator at this level to facilitate and coordinate service delivery at other levels.

- *District (BMU) level*. At district (BMU) level in integrated programmes, the district health officers are generally responsible for the operation of all public health programmes within their geographical area of responsibility, including TB training, supervision, drug supply and monitoring. Depending on the workload, one or more staff may be dedicated to TB control activities, or one staff member may be responsible for the activities of more than one programme.

- *Peripheral level*. The director of the peripheral health facility is responsible for service provision and staff management. TB care is usually provided by a number of general health workers. If the workload is high, TB care may be assigned to specific staff for better organization and training, or shared between several trained people to ensure continuation of services during staff absences.



BOX 10.1

ORGANIZATIONAL STRUCTURE OF A TYPICAL NATIONAL TUBERCULOSIS CONTROL PROGRAMME (NTP)

Central unit, including national TB reference laboratory, with NTP manager, technical officers and support staff

Regional/provincial coordinators specific for TB control, including regional reference TB laboratory

District (basic management unit) coordinators specific for TB control or with multiple responsibilities, including TB laboratory services

Health service delivery points – TB services, including laboratory, integrated into general health services

The central, regional and district levels are responsible for the managerial components of the programme, while the peripheral level of health facilities delivers programme services to the population. Good coordination between staff at each level is essential, as well as between all relevant public and private health-care providers delivering TB diagnosis and treatment

services. TB control staff at central and intermediate levels oversee the implementation of technical policies, design the planning framework, evaluate results, coordinate TB control activities with other programmes, agencies and institutions, and provide expert guidance to the district health team. Staff functions in the NTP should be clearly defined for each level.

Country coordination mechanisms (e.g. interagency coordination committees or national Stop TB partnerships) are being established in many countries to address the increasing need to coordinate activities with other programmes and with local and international partners. TB control programmes should establish collaborative mechanisms with national HIV control programmes, often through a national TB/HIV working group.

10.2 Functions of national tuberculosis control programmes

The overarching function of the NTP is the organization and delivery of TB care and prevention services to detect and cure all people with TB. Table 10.1 shows the core functions of the NTP at different levels of the health-care system.

TABLE 10.1 MAIN FUNCTIONS OF THE NATIONAL TUBERCULOSIS CONTROL PROGRAMME (NTP) AT DIFFERENT LEVELS

	Level	
National	**Provincial/ regional**	**District (basic management unit – BMU)**
Formulating policies and strategies: NTP manual	Contributing to development of national policies and strategies	Contributing to development of national policies and strategies
Planning and budgeting activities for TB control	Planning and budgeting activities for TB control	Planning and budgeting activities for TB control
Planning human resource development, including links with medical, nursing and laboratory technician schools	Planning human resource development	Planning and managing human resources
Producing and updating training Materials; conducting training for provincial/regional officers	Conducting training of district officers	Conducting training of local staff, including of clinical staff and community treatment supporters
Supervision of and technical support to provinces/regions	Supervision of and technical support to districts/BMU	Supervision of and technical support to clinics
Coordinating activities undertaken by different ministries, programmes, sectorsand partners	Coordinating activities undertaken by different programmes and partners	Coordinating activities undertaken by different programmes and partners
Assisting departments in the ministry of health to define specifications of and needs for medicines, laboratory materials and equipment and supplies	Supply and distribution of medicines and other commodities to districts/ BMU	Supply and distribution of medicines and other commodities to clinics
Coordinating laboratory activities with programme needs	Coordinating laboratory activities with programme needs	Coordinating laboratory activities with programme needs
Monitoring and evaluation (data management), including assessment of programme progress against objectives/targets	Monitoring and evaluation of district/BMU results	Recording and reporting; monitoring and evaluation
Advocacy, communication and social mobilization; engaging civil society	Advocacy, communication andsocial mobilization; engaging civil society	Advocacy, communication and social mobilization, including civil society and community involvement in support to patients
Operational research	Operational research	Contributing to operational research activities

A comprehensive approach to TB control requires an adequately and appropriately staffed central TB unit. The ministry of health should ensure that this unit has a multidisciplinary team including, as a minimum, a programme manager, a logistics officer and an

epidemiologist/statistician. In large countries, the team should also include staff responsible for training and ACSM, and for supervising and monitoring activities at regional and district levels. Staff responsible for public–private mix (PPM), drug-resistant TB management and TB/HIV collaborative activities may also be needed in some countries. In small countries, and in larger countries with a low TB burden, the team may also be responsible for other disease control programmes. The head of the national TB reference laboratory should be a member of the central unit, whether or not the laboratory is under the administration of the ministry of health.

A full-time regional TB coordinator (for a region, or for a province or state in federal government structures) should oversee the regional TB programme. The head of the regional TB laboratory will be a member of the team. In large regions, the regional TB coordinator will need the support of programme supervisors and staff for logistics and statistics.

The district (BMU) is the most peripheral managerial level within the public health-care system. Usually, it has responsibility for a population of 100 000 to 500 000 in an area, municipality, circumscription or city ward. The district TB coordinator in the BMU, who may also be responsible for other disease programmes, is under the supervision of the district, medical officer in charge of the BMU. The district BMU level initiates or expands TB control programme implementation in the district health facilities of the area and monitors its implementation at peripheral level.

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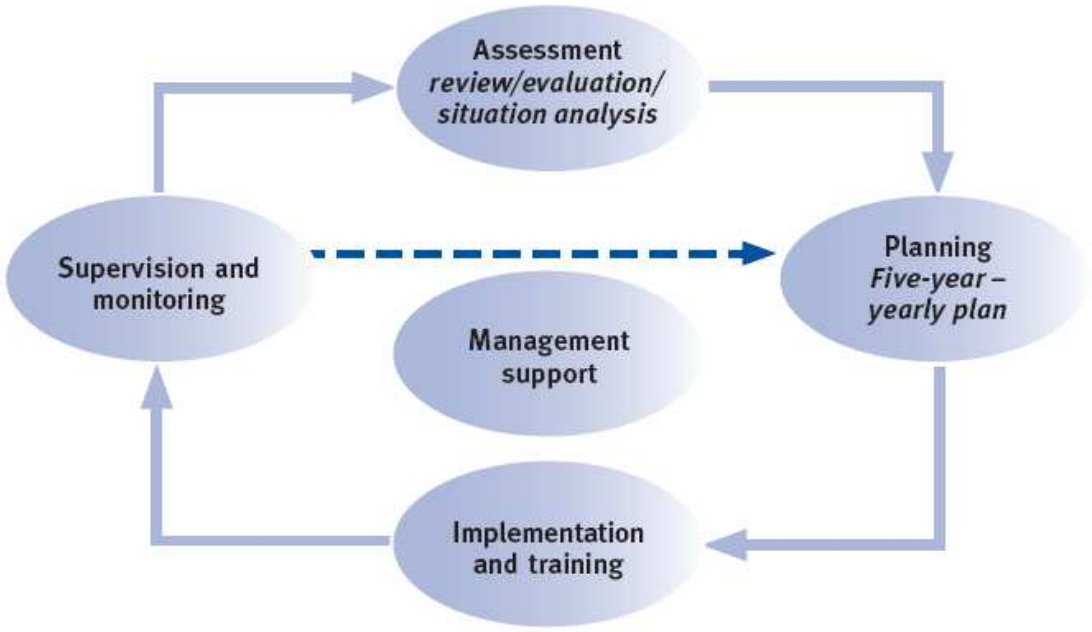
Chapter 11 Management cycle

The public health management cycle below illustrates how the different components of TB control, assessment, planning, implementation and monitoring/supervision are linked (Figure 11.1).

FIGURE 11.1 COUNTRY-LEVEL SUPERVISION AND MONITORING AS PART OF THE MANAGEMENT CYCLE



NTPs should periodically: (i) decide whether the national strategy to control TB is appropriate to current conditions or in need of revisions, additions, etc.; (ii) assess whether the strategy is effective and uses the available technology in the most efficient way; (iii) estimate the future needs and investment required to expand or change the strategy; and (iv) introduce new technology or new approaches as necessary. This process of strategic planning usually takes place every five years and results in a medium-term strategic plan (MTSP). The

plan has policy implications, guides implementation of the programme and serves to obtain internal and external resources.

As well as the MTSP, an annual implementation plan defines precisely the objectives and activities to be carried out during the year, together with a detailed budget.

The same cycles occur at international level. A medium-term global plan is developed by WHO and multiple partners who commit their support. Each institution carries out its own annual plan of activities with available resources, in support of national programmes and global initiatives.

11.1 Planning

11.1.1 Medium-term strategic plan

Most countries have adopted and implemented the DOTS strategy throughout their territory. Plans include maintaining and improving the quality of activities in the BMU and health facilities covered. For a comprehensive approach to TB control, the country strategic plan should include activities for all components of the Stop TB Strategy.

The MTSP specifies the country's objectives and targets for the NTP in line with global objectives and targets, usually for a period of five years, consistent with government health policies and with the overall health development plan of the country. The MTSP should be developed with inputs from all appropriate stakeholders, such as relevant departments of the

ministry of health (planning, financing, human resources, regulation/legal, curative services/hospital management, health information system, public health laboratory, health education, HIV/AIDS); social security services; other ministries under which special health services are organized; technical and other partners.

The MTSP sets out the national strategy and policies to achieve those targets, and indicates decisions on changes needed for implementation. Major activities for each of the components of the NTP are specified and budgeted for the next five years based on estimated needs to carry out planned activities; this allows resource mobilization to fill funding gaps. Use of the WHO standard TB planning and budgeting tool is recommended (see Chapter 19).
The MTSP aims to achieve expansion of activities to all components of the NTP and ensure political commitment with increased and sustained financing of infrastructure, human resources, supplies and equipment, and activities. An in-depth programme review should be organized in order to identify changes that need to be incorporated into the MTSP (see Chapter 18).

The main decisions based on the programme review are:

- to maintain or change specific strategies;
- to maintain or change technical and operational procedures;
- to expand programme activities in public health facilities and to other providers and sectors;
- to expand programme activities to collaborate in other areas and activities.

Programmes gradually evolve from a minimum package of essential interventions in public health facilities, to develop a full set of interventions covering all aspects of TB control and related diseases and delivered by multiple health providers and institutions.

The MTSP components specify the following:

- the country's goals and objectives for the NTP, consistent with national and international health and development goals;
- targets for the NTP in the medium term, based on the rates of current case detection and cure;
- national strategy and technical/operational policies for the medium term, indicating any policy changes and how they will be implemented;
- the major challenges for TB control in the country and strategies to address them;
- the main activities in the six key components of the Stop TB Strategy for the next five years;
- key managerial activities, quantified and with budget projections;
- priorities among the planned activities, to ensure implementation of the most essential interventions if the budget is not fully funded;
- a budget set out in broad categories, indicating the funding sources, funds that are available, committed or expected and the remaining funding gaps.

The MTSP will be implemented through an annual planning cycle, with more detailed budgeting and assignment of responsibilities.

11.1.2 Implementation plan

The next step in the planning process is to prepare the annual implementation plan. This plan should specify the activities to be undertaken during the next year and their estimated cost, working towards accomplishing the MTSP. The annual planning process usually takes place before the end of the year, so that resources may be obtained and distributed for use when the next year begins. Since the results of the current annual plan are incomplete at that point, data for the first three quarters and for the previous calendar (or budgetary) year are available and serve to estimate expected achievements. The annual plan should include:

- targets for the year, which should be challenging but feasible;
- the annual budget, with responsible officer, place and date, by activity;
- resource mobilization (government and external support) for the following year.

The following activities are part of the planning process. They are carried out at national level by the central NTP unit, and result in a plan that should be approved by the authorities and become part of the general plan and budget of the ministry of health. The plan should specify the sources of funds and the probability of financing. Essential activities should be based on secure funding.

(i) Analyse the information and assess the achievements of the NTP during the current year. The main sources of data are the quarterly reports from districts and regions, the regular monitoring of implementation of the previous plan, and any operational research carried out. The assessment examines the extent to which the NTP was able to:

- obtain political commitment with increased or sustained financing;
- expand case detection through quality-assured bacteriology;
- achieve the target for treatment success;
- maintain a regular drug supply and management system;
- monitor and evaluate the programme and measure impact;
- address TB/HIV, MDR-TB and other challenges;
- contribute to health system strengthening;
- engage all care providers;
- empower people with TB, and communities;
- enable and promote research, particularly programme-based operational research.

(ii) Develop a workplan for the following year, based on the MTSP and on evaluation of the previous year's results, as well as other information such as expected resources. Ideally the national plan is the consolidation of the district and regional plans, while in practice these plans are often developed in parallel and later consolidated.

(iii) Plan specific activities for the following year to implement changes in the NTP in accordance with the MTSP and with the achievements of the previous plan.

11.2 Monitoring and review

Monitoring is the observation of country programme performance to ascertain whether activities are accomplished according to guidelines and plans. Closely linked with supervision, monitoring is carried out at both the service delivery unit through direct contact

with health workers (supervision) and at the central managing office by examining periodic reports such as quarterly cohort reports on case notification, treatment outcomes and drug orders. Monitoring TB control is based on the standard recording and reporting system, standard indicators and direct contact with health workers.

Evaluation is a periodic assessment of progress towards operational targets and epidemiological objectives. Evaluation is undertaken after an interval of 12 months or longer. Closely linked to monitoring, evaluation is a process by which programme inputs, activities, process, outputs and outcomes are analysed and assessed against defined norms.
Monitoring and evaluation of programmes are conducted through three mechanisms: internal monitoring, external monitoring and programme reviews.

11.2.1 Internal (national) monitoring

National monitoring of planned activities and analysis of data are carried out every quarter at different levels, typically district, provincial and national levels. This monitoring is needed to identify areas of high and low performance and identify causes of poor performance. A well-maintained TB recording and reporting system allows health workers and TB programme staff to plan, monitor and evaluate services and drug supplies.

Monitoring activities aim to:

- ascertain whether activities, targeted performance indicators and milestones indicated in the five-year and annual plan are met on time and with required quality;
- gather and validate reporting and recording data;

- keep track of selected indicators on the performance and the conditions that influence performance;
- provide appropriate support to staff to improve implementation of the NTP.

Monitoring implementation and progress towards targets is facilitated when plans include a realistic schedule of activities for each component of the Stop TB Strategy and when a limited number of indicators offer a general overview of the TB control situation in a given setting. The list of selected indicators should refer to the component of the Stop TB Strategy, and a standard national TB manual should describe technically sound TB case management procedures for diagnosis, treatment, recording and reporting, drug management and laboratory supplies.

Monitoring includes site visits from the national level to intermediate and peripheral levels and from the intermediate to peripheral level. Site visits are planned to cover the whole country on a regular basis to assess consistent implementation of policies, timely completion of activities and progress towards targets, and to identify problems encountered by different levels.

At the end of the first quarter of the year, information from the previous year is available for the annual evaluation of the previous year's planned activities and analysis of annual trends. This information and analysis should be confirmed in an annual country report.

11.2.2 External (international) monitoring

External monitoring is undertaken to assess the NTP's performance from the perspective of TB experts working outside the country. External monitoring missions should be, as far as possible, joint missions of several partners with the NTP that are carried out once or twice a year. They use the national monitoring system with visits to several TB programme levels and care facilities and aim to identify general problems in the performance of the programme, and to identify solutions to poor performance. External monitoring missions include one or more international experts and one or several international partners.

11.2.3 Programme reviews

A programme review should be conducted regularly, normally once every 3–5 years. The objective is to analyse in depth the role, functions, structure and performance of the NTP. The additional objective is to review how the health systems operate with the focus on potential barriers to and opportunities for TB control within health systems reform.

The review is particularly important to help a country in the process of reorienting its TB control policies and replanning activities. A WHO guideline for the conduct of national TB control programme reviews is available. This complex exercise involves teams composed of experts from a wide range of national and external institutions such as WHO, technical agencies, NGOs, donor agencies, academic institutions and other partners, and includes a 2–3 month preparatory period. The review itself usually lasts 2–3 weeks. The first two weeks are devoted to briefing the review team, field visits and the presentation of field-visit reports.

The third week includes discussion of findings, formulation of recommendations and debriefing.

The outcomes of the review are:

- analysis of the epidemiological situation;
- analysis of the programme structure and resources, and the context of the general health-care system, health sector reform and role of hospitals, medical colleges, private sector and other entities involved in TB control;
- analysis of programme delivery and identification of achievements and constraints;
- recommendations for overcoming the problems identified.

TB control programme reviews are an important tool for securing government commitment and providing the basis for reorienting TB control policies and the development of an MTSP.

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Chapter 12 Programmatic management of drug-resistant tuberculosis

Prevention and control of MDR-TB are components of the Stop TB Strategy that should be integrated into the activities of NTPs in accordance with the strategy.

Despite their greater cost, diagnosis and treatment of MDR-TB are feasible and cost-effective, even in middle- and low-income countries. Untreated or improperly treated patients with drug-resistant TB are a source of ongoing transmission of resistant strains, resulting in added future costs and mortality. Incorrect use of second-line drugs to treat MDR-TB leads to further resistance to these drugs and development of XDR-TB. It is therefore imperative that second-line drugs are used appropriately.

Once drug-resistant strains are well established in a population, NTPs that use only standard short-course chemotherapy (SCC) will fail to cure a growing proportion of TB patients. Repeating SCC for patients infected with MDR-TB expands resistance to the drugs in use. Transmission of established drug-resistant strains in a population is also a significant source of new drug-resistant cases.

12.1 Addressing the sources of drug-resistant TB

The development of new cases of drug-resistant TB should be addressed urgently at the start of a drug-resistant TB treatment programme. The integration of DOTS and the management of drug-resistant TB may help identify and curtail possible sources of drug-resistant TB.

Possible factors contributing to the development of new cases of drug-resistant TB should be reviewed. Well-administered first-line treatment for susceptible cases using high-quality drugs is the best way to prevent acquisition of resistance for susceptible cases. Early identification of drug-resistant TB and prompt implementation of adequate drug-resistant TB treatment regimens (Category IV regimens) are essential to stop transmission of resistant strains.

12.1.1 The Green Light Committee Initiative

The Green Light Committee (GLC) Initiative promotes rational use of second-line drugs and helps to enable patients with, or at risk from, all forms of drug-resistant TB worldwide to receive proper diagnosis and timely, high-quality and effective treatment.

Through the GLC Initiative, NTPs have access to: (i) expertise in programmatic management of drug-resistant TB based on best available evidence and collective experience; (ii) high-quality drugs to treat drug-resistant TB at concessional prices; (iii) technical assistance through a wide network of technical partners; (iv) peer support and knowledge-sharing in communication with other GLC-approved programmes; and (v) independent external monitoring and evaluation.

12.2 Process for integration of management of drug-resistant TB

Implementing a drug-resistant TB treatment programme substantially strengthens overall TB control efforts for both drug-susceptible and drug-resistant cases. The management of drug-

resistant TB should be integrated into essential TB control services as rapidly as resources permit.

Integration of the management of drug-resistant TB within the NTP involves the following key steps:

- assessment of the political will of the government to deliver rational treatment to patients with drug-resistant TB (an essential prerequisite);
- assessment of the need to integrate drug-resistant TB management in TB control;
- design and implementation of a technical plan for management of drug-resistant TB and its stepwise integration within the TB control programme;
- monitoring and evaluation.

Provided the political will of the government to deliver rational treatment to patients with drug-resistant TB as part of the NTP is assured, the assessment of needs should be done, taking into account the following variables:

- the magnitude of the problem and the distribution of drug-resistant TB;
- prevailing patterns of drug-resistance;
- availability of second-line drugs on the pharmaceutical market;
- options and capacity for case-finding;
- options for proper treatment within the existing infrastructure of the health-care system, including the private sector;
- availability of laboratory capacity, including quality-assured culture and DST services;

- resources available for DOT over a prolonged period of time;
- availability of financial resources to integrate drug-resistant TB into the NTP;
- quality-assured standards of the laboratory network;
- availability of human resources and training needs based on a task analysis;
- existing legal framework for sourcing, importation, registration and distribution of second-line drugs;
- need for technical assistance.

The needs assessment will facilitate the design and implementation of a comprehensive plan to address the gaps identified, in terms of service delivery infrastructure and functions of the health-care system. Once the infrastructure is in place and the key functions are operating, a stepwise integration of drug-resistant TB control activities may be undertaken, giving initial priority to districts or administrative areas where integration is most likely to succeed.

The design and implementation of an NTP addressing drug-resistant TB may vary between and within countries, depending on the local needs and resources available. In settings where the private sector plays a significant role in the management of drug-resistant TB, the strategies developed should include PPM approaches (see Chapter 22). PPM approaches should be considered where (i) drug-resistant TB is generated through mismanagement of first-line drugs in the private sector, (ii) many of the drug-resistant TB cases are treated in the private sector and/or (iii) the private sector has access to or capacity for DST.

Whatever approach is taken, the essential requirements, such as quality-assured laboratories for diagnosis and monitoring, delivery of treatment under DOT, and use of quality-assured second-line drugs, should be met to ensure proper case management and prevention of emergence of resistance to second-line drugs.

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Chapter 13 Programmatic management of tuberculosis and human immunodeficiency virus

The programmatic management of coinfection with *M. tuberculosis* and HIV involves special challenges that call for effective collaboration between national TB and AIDS control programmes. Collaborative TB/HIV activities aim to decrease the burden of TB, HIV infection and AIDS in populations affected by both diseases; they are built on effective patient-centred collaboration between the two programmes (Table 13.1). A mechanism for collaboration between the TB and AIDS control programmes should be in place.

TABLE 13.1 WHO-RECOMMENDED COLLABORATIVE ACTIVITIES FOR TB/HIV CONTROL[a]

A.	**Establish the mechanisms for collaboration**
A. 1	Set up a coordinating body for TB/HIV activities effective at all levels
A.2	Conduct surveillance of HIV prevalence among TB patients
A.3	Carry out joint TB/HIV planning
A.4	Conduct monitoring and evaluation
B.	**Decrease the burden of TB in people living with HIV**
B.1	Establish intensified TB case-finding
B.2	Introduce isoniazid preventive therapy
B.3	Ensure TB infection control in health-care and congregate settings
C.	**Decrease the burden of HIV in TB patients**
C.1	Provide HIV testing and counselling
C.2	Introduce HIV prevention methods
C.3	Introduce co-trimoxazole preventive therapy
C.4	Ensure HIV care and support
C.5	Introduce antiretroviral therapy

[a] Adapted from *Interim policy on collaborative TB/HIV activities*. Geneva, World Health Organization, 2004 (WHO/HTM/TB/2004.330; WHO/HTM/HIV/2004.1).

Key activities for the programmatic management of collaborative TB/HIV activities include:

1. Creation of a joint national TB and HIV coordinating body working at regional, district and local levels (sensitive to country-specific factors), with appropriate representation of the TB and AIDS control programmes and of stakeholders including TB and HIV patient-

support groups and community-based organizations. The coordination body (which may be a committee, task force or group depending on country-specific factors) facilitates the creation of a favourable policy and programme environment, which includes the development of appropriate national policy defining the activities to be implemented in the country and operational guidelines, training manuals and protocols. For countries with concentrated and low HIV prevalence, priority settings with a high burden of HIV-associated TB (provinces, districts or facilities) should be identified. TB infection control in HIV and AIDS prevention, care and treatment settings should be prioritized (see Chapter 6).

2. Development of joint national strategic and operational plans that define the roles and responsibilities of each programme and the allocation of resources, including the deployment of sufficient human resources and capacity for health-care delivery to implement collaborative TB/HIV activities at all levels. The plan may be either separate or incorporated into national TB and HIV strategic plans with TB and HIV components. Training of health workers in programme management and clinical competencies is crucial and should be included in the operational plan.

3. HIV surveillance among TB patients in all countries irrespective of national adult HIV prevalence rates, in accordance with WHO guidelines.

4. Expedited diagnosis and treatment of TB in HIV-prevalent areas and among HIV-positive individuals, with intensified TB case-finding in all HIV counselling and testing,

AIDS care and treatment settings and among populations at high risk of HIV. A referral system should be established between HIV counselling and testing, AIDS care and treatment, and TB diagnostic and treatment centres. For countries with concentrated and low HIV prevalence the recommendations for the diagnosis and treatment of smear-negative pulmonary and extrapulmonary TB should be implemented in priority settings.

5. Provision of isoniazid preventive therapy by HIV service providers as part of the package of care for PLHIV when active TB has been excluded. Information about IPT should be made available to all PLHIV.

6. HIV testing and counselling offered to all TB patients regardless of the national HIV epidemic status. NTPs should either integrate provision of HIV testing and counselling in their operations, or establish a referral linkage with the HIV programmes to do so. All HIV-infected people who have confirmed TB should also be provided with HIV care, treatment and support services including ART.

7. Comprehensive HIV prevention strategies developed and implemented by NTPs for their patients targeting sexual, parenteral or vertical transmission, or referral linkage with HIV programmes to do so should be established. NTPs should provide harm-reduction measures for TB patients who practice injecting drug use, or should establish a referral linkage with HIV programmes to do so.

8. Establishment of a system to provide CPT by TB and HIV control programmes to eligible PLHIV who have active TB.

9. Agreement on a core set of indicators and data collection tools by HIV and TB programmes, and data collection for monitoring and evaluation of collaborative TB/HIV activities. The WHO guidelines for monitoring and evaluation of collaborative TB/HIV activities should be used as a basis to standardize country-specific activities.

10. Address key factors for acceleration of TB/HIV activities based on experience and best practice from pioneer countries in nationwide expansion of collaborative TB/HIV activities, as follows:

    - setting national targets for collaborative TB/HIV activities to facilitate implementation and help mobilize political commitment on the part of the TB and HIV control programmes;
    - creating a supportive policy environment with the development of appropriate policy and operational guidelines, training manuals and protocols in line with international guidelines;
    - engaging stakeholders through effective HIV/TB coordinating bodies at all levels to help coordinate the national response and accelerate the implementation;
    - expanding HIV testing facilities and allowing front-line TB clinicians and nurses to test not only confirmed TB patients but also those presenting with signs and symptoms of TB (“TB suspects”);

- intensive, continuing training and supportive supervision of health workers;
- implementing revised recording and reporting formats on collaborative TB/HIV activities to document progress in implementation. The inclusion of TB components in HIV registers and HIV components in TB registers in line with international guidelines is important;
- effective and constant supply of HIV test kits, drugs and other important commodities that are essential for accelerated implementation.

WHO guidelines

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Chapter 14 Laboratory services

Laboratory services, although crucial for national disease control programmes, are often the weakest link in the health system, receiving low priority and inadequate resources. For TB control, quality-controlled bacteriological examination is essential for the diagnosis and management of TB patients. Laboratory strengthening is a priority for the Stop TB Strategy, including improved access to and use of existing diagnostics as well as the development and implementation of appropriate new technologies.

The strategic orientations for laboratory strengthening focus on:

- improving smear microscopy;
- strengthening and expanding capacity for culture and DST;
- adapting and transferring existing technologies to resource-limited settings;
- contributing to development and testing of new diagnostic tools under field conditions.

14.1 Organization of TB laboratory services

TB laboratory services should be integrated within the national system of laboratory services. At the central level, the national reference laboratory is either located within the NTP or may be part of the general laboratory system with close links to the NTP. A full description of the organization of TB laboratory services is contained in *Laboratory services in tuberculosis control, Part I*.

At the regional and peripheral levels, TB laboratories are fully integrated with the reference hospitals, district hospitals and health centres. The laboratories at the regional and peripheral levels are multipurpose, with technicians performing tests for the diagnosis of a wide variety of diseases. Inclusion of accredited laboratories outside the public health sector (university, hospitals, private and NGO based) in the NTP laboratory network should be considered (see Chapter 22).

Efforts to improve the laboratory performance should be well coordinated to avoid fragmentation and the creation of separate disease-specific services. In high HIV-prevalent settings, HIV testing should be offered to TB suspects along with sputum examination. Based on national policies, HIV tests may be carried out in TB laboratories and/or by health-care providers.

14.2 Diagnostic procedures

14.2.1 Sputum smear microscopy

Early laboratory diagnosis of TB relies on the microscopic examination of respiratory specimens for AFB. The technique, although of limited sensitivity,[1] is relatively simple and inexpensive, and is currently indispensable in the detection of the most infectious cases of pulmonary TB. An internationally-agreed training package and external quality-assurance system for standard sputum smear microscopy is available.

[1] Microscopic detection of a single AFB in a sputum smear corresponds to a concentration of 10 000 bacilli/ml sputum; culture detects AFB at a concentration corresponding to 100 bacilli/ml sputum.

Fluorescence microscopy is more sensitive than standard light microscopy for TB diagnosis. Modern improved fluorescent microscopes equipped with a light-emitting diode (LED) offer a promising alternative to standard fluorescence lamps, avoiding the need for dark rooms. Their use is recommended where possible in laboratories examining more than 100 smears per day; this allows more rapid examination, decreased technician workload and improved efficiency of AFB detection.

14.2.2 Culture

Mycobacterial culture is much more sensitive than smear microscopy and provides a definitive diagnosis of TB. It is therefore seen as the gold standard for bacteriological confirmation. Culture on solid media, especially Löwenstein-Jensen and its modified version, is the most widely used technique. However, it has disadvantages owing to the length of time required (4 to 8 weeks) for growth of mycobacteria on a solid medium and delays in starting treatment while awaiting a confirmed diagnosis. The method requires a suitable infrastructure including biosafety measures, sound technical skills and motivation of laboratory personnel.

Culture on liquid medium is the standard method for TB diagnosis and patient management in high-income countries. Culture on liquid medium is more complex than on solid medium but it is rapid and can provide results in about 10 days. With this method, special precautions are needed to avoid bacterial contamination and isolation of non-tuberculous mycobacteria. Strengthening the capacity to perform culture on liquid media at country level is necessary to adequately address MDR-TB and XDR-TB.

14.2.3 Drug susceptibility testing

DST, performed on either solid or liquid media, provides bacteriological confirmation of drug-resistant TB. WHO recommends carrying out DST for first-line and second-line anti-TB drugs to detect MDR-TB and XDR-TB respectively (see Chapter 1). Laboratory services for culture and DST should be introduced in a phased manner at appropriate referral levels of the health system. Efforts to expand the use of culture and DST should be based on a well-performing laboratory network that maintains a high quality of service by regular training, supervision and support, and motivation of laboratory staff.

In 2007, the World Health Assembly called for enhanced laboratory capacity to provide rapid DST for all cases of culture-positive TB (WHA60.19). The needs for culture and DST in different epidemiological settings have been estimated on the basis of optimal recommendations, recognizing that implementation in many settings will be achieved only gradually. Further planning for wider implementation of culture and DST will be carried out and reported on by WHO.

Recommendations differ for new cases according to the country's epidemiological situation, defined as follows: (i) high MDR-TB burden countries where MDR-TB cases together contribute 85% of the global MDR-TB burden; (ii) high HIV prevalence settings (countries, districts, counties or selected facilities such as referral hospitals) where the HIV prevalence rate among pregnant women or the general population is at least 1%, or HIV prevalence among TB patients is at least 5%; (iii) all other countries/settings.

Culture and DST are recommended for all re-treatment and chronic TB cases and for children with TB. Second-line DST is recommended for all MDR-TB cases. The overall aim is to offer universal access to all culture and DST services by 2015.

14.2.4 Detection of latent TB infection

Tuberculin skin test. The diagnosis of latent TB infection generally depends upon the standard TST, despite limitations concerning the reliability of its interpretation. Technical aspects of tuberculin administration and the method of reading may lead to false negative results, while false positive results may be related to prior immunization with the BCG vaccine or exposure to environmental mycobacteria. Interpretation of the tests should strictly follow WHO recommendations detailed elsewhere (see *Guidance for national tuberculosis programmes on the management of tuberculosis in children*; *TB/HIV: a clinical manual*; and chapters 4 and 5).

Interferon-gamma release assays. Blood tests detecting the release in vitro of interferon-gamma (IFN-γ), or measuring the number of T-cells producing IFN-γ on contact with secreted antigens of *M. tuberculosis*, have been developed and are commercially available. The selected antigens used in these tests are highly specific for tubercle bacilli, since they are absent from all BCG strains and from most environmental mycobacteria. Consequently, the occurrence of false positive results is minimized. However, as with TST, a negative IFN-γ test is not sufficient to rule out latent TB infection, especially in cases of immunodeficiency caused by HIV infection or other co-morbidities. In several TB low-incidence countries,

IFN-γ tests are recommended in place of TST. The potential public health role of these tests in high-burden countries remains to be evaluated.

14.2.5 HIV testing

HIV testing should be routinely offered, along with sputum examination for AFB in HIV-prevalent settings, for patients presenting with a cough of 2–3 weeks' duration. A person with unknown HIV status (e.g. because of unavailability of HIV test kits or refusal to be tested) may be classified as HIV-positive if there is strong clinical evidence of HIV infection.

14.2.6 New technologies

New TB diagnostic tests are needed to provide sensitive, specific and timely detection of both drug-sensitive and drug-resistant TB and to perform equally well in TB/HIV coinfection. Several products that may meet these demanding criteria are under development. New tools should be tested through research that provides reliable data on sensitivity, specificity, positive and negative predictive value per test and per patient, conducted in high-burden countries under field conditions.

Prior to wide implementation of a new test, countries should design an operational research protocol and field test the new tool in order to define logistics, infrastructure and equipment needs, technical constraints, training needs and potential scope of implementation. The decision on whether to implement a test should be based on consideration of its advantages

and limitations. The impact of a change of testing policy on the current laboratory diagnosis of TB or drug resistance should be addressed with the NTP.

14.3 Laboratory safety

To obtain reliable results, all laboratory techniques including microscopy, culture and DST should be performed by appropriately trained staff working in properly-equipped safe laboratories. Occupational health requirements should be applied (see section 2.11). Training in safety measures should be part of the basic training curricula for laboratory personnel. Training should include information on exposure to TB bacilli, control of laboratory hazards and safe laboratory procedures. Exposure to biohazards differs according to the type of services performed:

- In laboratories where sputum samples are handled for microscopy only, exposure to infectious particles generated from specimens is low due to the high viscosity of sputum. In these laboratories, adequate protection of laboratory staff is provided by appropriately directed airflow ensuring sufficient air changes in the room.
- Specimen processing for culture purposes should be performed in biological safety cabinets (BSCs), at least in Biosafety Level 2 (BSL2) facilities. However, because culture manipulation represents a high biohazard risk with exposure to high concentrations of TB bacilli, identification and DST activities should be performed in BSL3 facilities by appropriately qualified staff in accordance with BSL3 practices. Upgrading to BSL3 should be planned and implemented according to a short-term

plan and with identification of adequate resources; this is a responsibility of the country.

- For most high-burden countries, there are major constraints to the successful establishment, staffing and maintenance of BSL3 laboratories. Any proposal to create a BSL3 laboratory should take account of all the structural, logistic and staffing requirements and associated costs over time.
- Laboratories that send cultures of *M. tuberculosis* to other laboratories should comply with the (national and) international regulations on the transport of dangerous goods (see Chapter 20).

14.4 Quality system

The availability and quality of bacteriological diagnosis of TB relies on the capacity of the NTP to support, train and monitor the testing performance of individual laboratories. The NTP and NRL are responsible for implementing a quality system (QS) covering all the diagnostic tests and the laboratories involved in the diagnosis of TB.

- QS consists of internal quality control (QC), assessment of performance using an external quality assurance system (EQA) including on-site evaluation with on-site supervision based on blind rechecking for microscopy and panel testing for DST, and continuous quality improvement (QI) of laboratory services.

- QC includes all means by which the laboratory controls its operations, e.g. the use of standard operating procedures (SOP). This includes checking of equipment, supplies, testing, recording and reporting.
- EQA using a blind rechecking system should be performed for all TB diagnostic tests including sputum microscopy and DST.

Regular on-site evaluation (supervision), using a standardized checklist, is an important tool to assess laboratory performance. Improvement is facilitated by a regular and timely feedback mechanism with identification and correction of shortcomings.

14.5 Public–private mix for laboratory services

Many countries have a large private medical sector serving a significant proportion of TB cases. Private care providers often depend on private laboratories for smear microscopy and, in some places, mycobacterial culture and DST. If linked appropriately to NTPs, private laboratories may potentially contribute significantly to improving access to TB diagnosis. For effective collaboration, verifiable mechanisms for ongoing supervision and EQA of participating private laboratories services are essential.

Ways to engage private laboratories in TB control will vary in different settings. It is important to have an explicit national policy that facilitates collaboration with private laboratories. The NTP should define the tasks that the individual laboratories will undertake and the support they will receive from the NTP. A complete list should be compiled of

laboratories providing TB diagnosis in the country. Local TB units should know the number, locations and services provided by private laboratories operating in their areas.

It is advisable to work initially with a limited number of private laboratories depending upon their workload, willingness to participate, the local need and the capacity of the local TB unit to train, supervise and undertake quality assurance of participating laboratories. The experience and the results of collaboration should form the basis of a phased and sustainable scale-up of private laboratory involvement in TB control (see also Chapter 22).

14.6 Resources

14.6.1 Human resources

Estimation of the number of laboratory staff required is based on the workload and range of tasks to be carried out. Laboratory staff should be made aware of their important role in the control of TB and treated as full partners: this is essential to maintain motivation and an effective relationship with the NTP. Training programmes should be in place to improve and update the technical and managerial skills of laboratory staff, with a regular follow-up system to monitor and evaluate trainees.

14.6.2 Financial resources

Despite the availability of substantial international funds for TB control, laboratory needs have often been underestimated. Funding proposals for TB control should always include the financial needs for the strengthening of laboratories, as defined in collaboration with the

members of the NRL. Laboratory staff, equipment, maintenance, supplies, quality assurance, supervision and training are essential elements of the laboratory service and should be given appropriate consideration.

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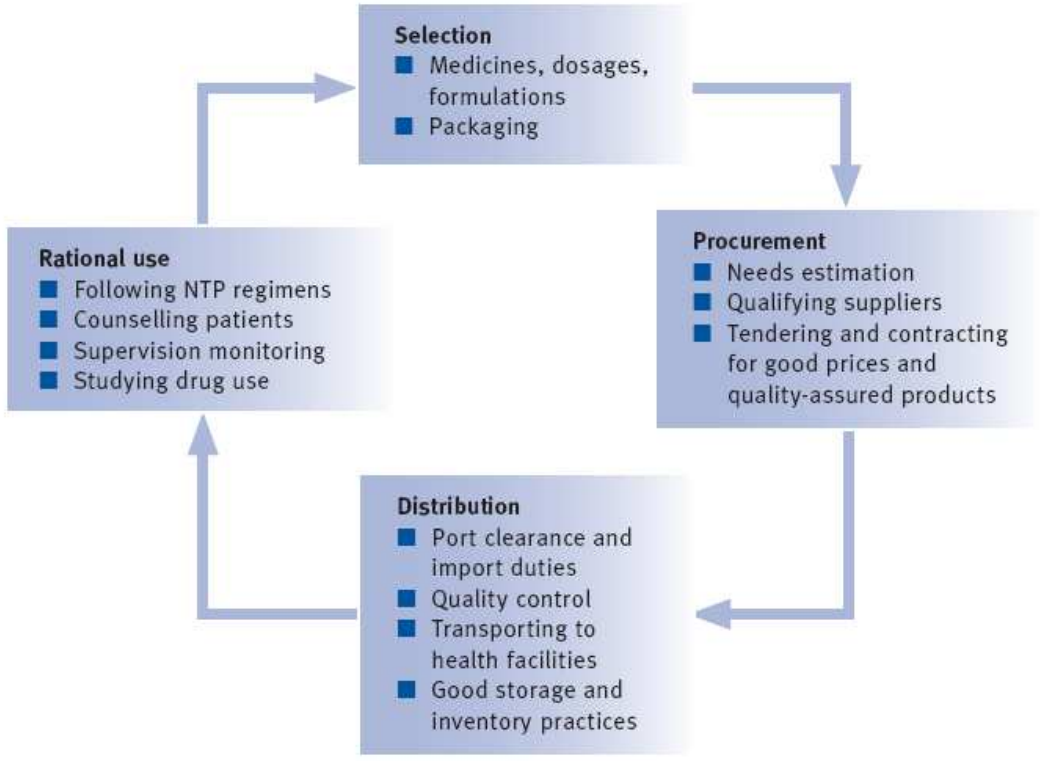
Chapter 15 Management of antituberculosis drug supplies

Good TB control requires the availability of adequate quantities of medicines whenever needed by patients and health workers. All aspects of drug management should therefore be included during the TB control planning and implementation processes. Drug management involves close collaboration with the national essential medicines programme; in many countries, anti-TB drugs are co-managed by the essential medicines programme.

As shown in Figure 15.1, drug management includes essential steps in the selection, procurement, distribution and rational use of drugs.

FIGURE 15.1 DRUG MANAGEMENT PROCESS



15.1 Selection of anti-TB drugs

WHO recommends five essential medicines for first-line antituberculosis treatment: isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin. These medicines are available in different formulations and packages, and several considerations are involved in their selection:

- using blister packs for better handling and inventory control;
- using FDCs of two, three or four medicines, to reduce the risks associated with monotherapy;
- using patient kits to avoid treatment interruptions, simplify handling and improve patient adherence.

The selection process for second-line medicines used to treat drug-resistant TB cases varies considerably (see Chapter 2). Whichever formulations are chosen, the NTP manager should ensure that all they are all included in the national list of essential medicines.

15.2 Procurement of anti-TB drugs

Drug procurement should take account of the following key issues:

- Accurate demand forecasting of anti-TB drugs, i.e. correct quantification of the needs for drugs for a specific period of time, is an essential prerequisite for ensuring an uninterrupted supply.

- Effective management of procurement ensures the availability of the drugs selected in the right quantities, at the right time, at affordable prices and at acceptable standards of quality.

- Annual centralized procurement is the most efficient way to build up the confidence of suppliers and draw prices and costs down, through the use of a standardized package of procurement bidding documents and bulk purchase of medicines. It is also easier to control and factor in the lead times of suppliers.

- Through its prequalification scheme, WHO regularly updates a list of manufacturers whose anti-TB drugs have been ascertained to be of acceptable quality (i.e. prequalified).[1]

- The most competitive prices for first-line anti-TB drugs are obtained from the GDF, which is an initiative of the Stop TB Partnership to increase access to high-quality anti-TB drugs.[2]

- The GDF offers a reliable source of pooled procurement of second-line drugs. Countries should apply to the Green Light Committee to benefit from quality-assured drugs, preferential prices and a reliable source, together with regular external monitoring/evaluation and technical assistance to conduct a management programme for drug-resistant TB.

[1] The list is available at http://www.stoptb.org/gdf/
[2] See http://www.stoptb.org/gdf/

- All drugs used in a regimen for anti-TB treatment should meet the WHO recommended standards for safety, efficacy and quality. Quality also depends on a set of standards maintained throughout the entire process of manufacture and distribution.

15.3 Distribution and storage of anti-TB drugs

Distribution and storage of drugs should take account of the following key factors:

- Management of drug importation requires that all port and customs clearance forms are duly completed. The formalities involved depend on whether or not the drugs have been registered in the importing country (see Chapter 20). In many countries it is possible to obtain an exemption to import drugs that are not locally registered on the basis of their public health importance.

- Some countries place duties on imported products, but anti-TB drugs may be exempt when they are considered as humanitarian assistance, provided all required paperwork has been done correctly.

- To preserve quality, the drugs should be transported and stored by the suppliers and the TB control programme, following the recommendations specified by the manufacturers regarding temperature and humidity. Good storage practices should be in place at all levels, which requires that staff are appropriately trained and storage conditions adequate.

- In peripheral centres where storage conditions do not meet recommendations on temperature and humidity, it is advisable to organize frequent supplies of limited quantity in order to minimize the duration of storage under suboptimal conditions.

- A regular system of distribution for drugs and commodities should be in place from the central level to the regions and peripheral levels, in order to ensure an uninterrupted supply.

- An inventory management system needs to be set up in order to ensure a safety stock and optimal stock movement, and provide an accurate source of information for drug-demand forecasting.

- Regular physical quality checks when drugs arrive, and at all stages of the drug supply cycle (warehouses, health centres) should be performed. Where testing laboratories are not available in the country, these services may be contracted to the closest external laboratory.

- In health facilities, the organization of complete courses of treatment in individual containers (patient kits) avoids treatment interruptions and improves patient adherence.

15.4 Rational use of medicines

Access to anti-TB medicines must be accompanied by measures to ensure their rational use (see Chapter 2). This also involves actions to limit misuse of first- and second-line drugs outside the NTP. Anti-TB medicines can often be bought over the counter in private pharmacies, and/or are prescribed and dispensed by a wide range of providers who do not

follow national guidelines and who do not apply appropriate measures to ensure treatment adherence.

Interventions to reduce irrational drug use outside the NTP involve improved and enforced regulations on drug prescription and dispensing. This requires collaboration with the national drug regulatory body, other departments of the ministry of health, other ministries, and professional associations of prescribers and pharmacists. In addition, public–private mix approaches should be applied to improve rational use of TB medicines throughout the health system (see Chapter 22).

WHO guidelines

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Chapter 16 Supervisory support to basic management units

This section describes the supervisory and monitoring activities that occur when external or in-country supervisory visits to health facilities are conducted. In theory, supervision, monitoring and evaluation are distinct managerial steps. In practice, these three activities are closely linked, with considerable overlap and a common approach. Supervision involves mostly in-country activities, conducted from upper to lower levels of the health system by clinicians and/or managerial TB staff.

Supervision is the observation of health workers in their workplace, performed on a regular basis (every 1 to 6 months), with the aim of developing their knowledge, perfecting their skills, solving problems, correcting errors, improving attitudes towards their work and increasing staff motivation. It is also termed “on-the-spot training”. Supervision should be educative and supportive, not punitive. The supervisory relationship should be positive and encouraging for the supervised staff.

Supervision and monitoring can be of great benefit for the improvement of programme performance. The objectives of supervision, whether performed through external monitoring mission or during routine supervisory activities by NTP, are similar, i.e. to ensure the quality of the work according to the programme’s planning and implementation targets and to the recommended practices. Good TB control depends on proper and regular monitoring and supervision.

Supervisory visits aim to:

- reinforce and promote the use of good diagnostic, treatment and drug-use practices, as detailed in the national guidelines;
- help health workers to transfer learning skills to clinical work in facilities;
- identify problems faced by health workers in managing TB cases so that they can be solved without delay on the spot or with other partners during meetings;
- stimulate health worker team spirit and motivation;
- provide technical advice and guidance to health workers in order to enhance their knowledge and encourage a positive attitude and good practices;
- become informed of the opinions of TB patients concerning service delivery and expectations.

Supervisory visits should involve five main units: the laboratory facility, the central drug pharmacy, the hospital ward, general and TB specific outpatient facilities, and the office where records and reports are kept.

During field visits, supervisors make observations and carry out interviews, sometimes with the aid of a supervisory check list. However, much of what supervisors do is problem-solving and training. Problem-solving and on-the-spot training should always refer to the national guidelines and national training document. If problems cannot be corrected on the spot, the supervisor should make a written record, identify potential causes and propose solutions.

The key components and subcomponents of the Stop TB Strategy should be considered during supervision and monitoring activities. Priority should be given to serious weak points in order to focus on problem-solving. The main function of the field visit is not only to gather quantitative data, which should be available before the visit starts, but also to observe the organization and delivery of TB services, to discuss problems and to assess the validity of the data.

Supervision is mostly provided by one qualified and knowledgeable member of the TB programme staff. Additional members of the supervision team may include the medical supervisor, the laboratory supervisor, pharmacists, nurses and trainees.

Supervision should be carried out at all levels of the health infrastructure, with regular visits to all health services. Visits should be arranged to selected institutions, organizations and individuals, and to TB patients eventually at home at the peripheral level. The supervisory team should prepare a draft report during the visit and provide it to the TB staff responsible for immediate action. The main recommendations should be discussed and, if possible, agreed upon during the visit. The report should be short and may include:

- actions taken since the last visit;
- main achievements and constraints observed during the visit;
- recommendations and proposed next steps before the next visit to overcome problems or improve programme performance.

A five-year plan and an annual operational plan of work facilitate the management process by providing references and standards for comparison during each management period, including supervisory and monitoring activities.

A regular monitoring and supervision mechanism should be put in place to ensure that activities are conducted as planned in the five-year plan and the annual operational plan, respecting good practices recommended in the technical guidelines.

The preparation of new mid-term and long-term plans is based on a periodic and regular evaluation of the programme.

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Chapter 17 Development of human resources

Human resource development (HRD) is a key element in overall health systems development. The quality of service delivery, including of interventions for comprehensive TB control, depends to a large extent upon adequate numbers of staff and their performance, supported by the availability of sufficient facilities, equipment, drugs and other commodities. The performance of personnel depends on various factors such as motivation, training, supervision, salaries and working conditions, all of which require carefully formulated and implemented health workforce policies.

Health workforce development for TB control is concerned with the different functions involved in planning, managing and supporting the professional development of the health workforce for comprehensive TB control within overall health workforce development. The strength and sustainability of NTPs depend on timely, adequate and ongoing recruitment, training, deployment, motivation and management of health workers to ensure that the Stop TB Strategy can be implemented in the context of national guidelines.

There is today a substantial shortage of health workers to meet global health needs. However, shortages are not universal or even uniform across low-income countries or even within countries. An inadequate skills mix, distributional imbalances, unfilled vacancies and poor working conditions exacerbate the problem. This shortage is in many places a major constraint to achieving the health-related MDGs.

The long-term goal for HRD for comprehensive TB control is to reach and sustain a situation where:

- health workers at different levels of the health system have the skills, knowledge and attitudes (professional competence) necessary to successfully implement and sustain comprehensive TB control services based on the Stop TB Strategy;
- a sufficient number of health workers of all categories involved in comprehensive TB control are available at all levels of the health system, with the needed support systems to motivate staff to use their competencies to provide high-quality TB services for the entire population according to their needs.

Effective strategies provide the road map for achieving and sustaining the goal for HRD for comprehensive TB control, enhancing the performance of the health system, even under difficult circumstances. Such strategies include, but are not limited to, the list below. These strategies apply to all countries/areas. However, depending on the country-specific situation, the activities planned under each strategy will differ. The key strategies and implementation approaches are:

- contributing to overall workforce planning and policy development;
- organizing in-service training (clinical, laboratory and managerial) for all health workers involved in TB control, including private providers engaged in programme activities:
  - initial training in all aspects of basic DOTS implementation for existing staff and new recruits at all levels;
  - initial training on TB/HIV and MDR-TB;

  - retraining (major performance problems that may be addressed through, for example, a formal training course);
  - on-the-job or refresher training (minor performance problems that may be addressed during a supervisory visit);
  - continued education (to build skills and knowledge);
  - training/orientation of all public and private providers;
  - advanced training on management aspects (health financing, leadership/governance, business planning, organizational development);
- strengthening preservice training (basic training) for physicians, nurses, laboratory technicians and other health workers involved in the implementation of TB control;
- engaging in strategic partnerships for health workforce development for comprehensive TB control with, for example:
  - training divisions/institutions;
  - other in-service training programmes, e.g. HIV;
  - ministry of education and other relevant ministries;
  - professional associations;
  - private sector including NGOs;
  - bilateral and international organizations;
- contributing to integrated personnel management systems at all levels to foster adequate workforce planning, recruitment, hiring, deployment and retention;
- monitoring and supervising health worker performance:
  - to detect and remedy performance deficiencies;
  - to identify new staff in need of training;

– to identify additional staff needs.

The management and implementation of strategies should be made within the context of the Human Resources for Health Action Framework, which addresses the health workforce crisis. The framework includes six action fields: policy, finance, education, partnership, leadership, and human resource management systems; and four phases of the action cycle: situation analysis, planning, implementation, and monitoring and evaluation. http://www.who.int/hrh/tools/en/

To ensure a comprehensive approach to the HRD challenge, all action fields and phases of the action cycle will eventually need to be addressed. However, based on a particular area of need or NTP responsibility, any action field or phase may be selected for in-depth analysis and planning.

Table 17.1[1] describes the role and functions for different aspects of HRD for comprehensive TB control, based on the action framework. To enable these functions to be carried out within the NTP, programmes should establish the organizational structure at the central level. This includes, but is not limited to:

- assigning a dedicated focal person for HR in the NTP. In larger countries, this corresponds to a full time job. A focal point may also be needed at state/provincial level;
- appointing an HR coordination group with representatives from training institutions, health workers, concerned professional organizations, and other disease control programmes;
- determining the roles and functions of HR management at subnational levels.

[1] *Planning the development of human resources for health for* implementation of the Stop TB Strategy: a manual [in press]. Geneva, World Health Organization, 2008

TABLE 17.1 ROLE AND FUNCTIONS OF NATIONAL TUBERCULOSIS CONTROL PROGRAMMES (NTPS) FOR HUMAN RESOURCE DEVELOPMENT (HRD)

Action fields	National tuberculosis control programme
Policy	Assesses need for HR policy revisions to enable implementation of the Stop TB Strategy (e.g. task shifting; hiring of additional staff above current staffing stands; incentives for disadvantaged geographical placements; HR needs in special situations; needs for and participation in special tasks forces and coordination groups)
Finance	• Aligns with and uses TB-specific funds to support overall health workplace development • Ensures the allocation of TB specific funds; enables implementation of the strategic plan for HRD for comprehensive TB control • Ensures donor coordination for financial support to the implementation of the strategic HRD plan for comprehensive TB control
Education, including pre-service (basic), postgraduate, in-service and continuing education	• Develops/revises in-service training programmes for different categories of health workers involved in the implementation of a comprehensive NTP according to the functions • Develops/revises training materials for the above • Ensures that all continuing education is based on health service needs for TB control, is competency based, and follows NTP guidelines • Ensures objective competency-based evaluations systems are in place and used for all training programmes • Selects and trains course facilitators for the different training programmes (paying particular attention to the technical and educational competencies of the future facilitators, as well as the ability to encourage course participants to develop skills in independent thinking and problem solving) • Organizes training courses (long term as well as short term) in close collaboration and coordination with other priority health programmes and interventions • Involves existing training institutions to strengthen educational quality of training activities • Ensures continuous learning for all heath workers involved in the implementation of the NTP • Establishes the organizational structure for follow up after training • Trains supervisors for follow up of staff training • Ensures pre-service training programmes meet the competency needs for the implementation of the NTP
Partnerships	Ensure linkages with other public sector, private sector and community networks with common linkages to TB; for example, HIV national programmes, medical associations, faith-based organizations, WHO, KNCV, IUATLD
Leadership	• Provides visionary leadership and advocacy for TB programme needs • Ensures leadership development for managers at all TB programme levels; empowers managers to solve problems at service delivery level, ensuring needed resources are available • Provides supportive supervision to develop workplans and monitor performance

Continued

Table 17.1 *Continued*

Human resource management	**Personnel management** • Assesses staffing needs at all levels, including the central level, for the implementation of the NTP • Contributes financial resources to staff retention strategies and incentive packages for rural postings • Determines minimum data requirement for adequate HR management • Ensures all HRD activities conform to overall HR management systems and policies currently in place • Communicates staffing problems (e.g. vacant posts, severely understaffed health centres) identified during supervisory visits **Performance management** • Updates as necessary, and list functions and tasks by level and by professional category covering all components of the NTP • Develops/revises job descriptions for staff involved in TB control to correspond with current policies and recommendations for TB control, e.g. the introduction of management of MDR-TB • Coordinates capacity development (competence and staffing) for supportive supervision – for implementation of the Stop TB Strategy – with other high-priority programmes • Contributes expertise and resources to the development and implementation of strategies for staff motivation and retention (not only financial)

The table indicates the guiding principles; the overall structure and situation will vary from country to country. HRD functions within the NTP are carried out in close collaboration and coordination with the overall HRH department to ensure optimal efficiency and results. This should also ensure that HRD activities within the NTP are in harmony with the overall HRH policies of the ministry of health, and ensure that the NTP HRD plans are integral parts of overall HRH plans.

NTPs need to develop and support strategic approaches to staffing, competence development and creation of an enabling environment for all staff involved in the implementation of TB control, based on the outline above, as well as coordinating their efforts with overall health workforce development. HR plans should be integral parts of the two types of plans previously described: the strategic medium-term plan and the annual implementation plan.

The strategic plan focuses on long-term direction and provides overall guidance for implementation and financing to ensure the achievement of the goal of an adequate, competent and performing health workforce. It provides guidance for the annual implementation plans.

The annual implementation plan should be short term, tactical, focused, feasible and measurable. It should include short-term objectives and activities needed to progress towards the goal of an adequate and competent workforce.

International organizations support national TB HRD by providing technical and financial assistance, developing generic training modules and manuals, and organizing international training courses.

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Task analysis: the basis for development of training in management of tuberculosis. Geneva, World Health Organization, 2005 (WHO/HTM/TB/2005.354).

Chapter 18 Monitoring and evaluation of programme performance

Monitoring and evaluating the performance of TB control programmes involves assessing activities, monitoring costs and expenditure, determining the extent of programme coverage and evaluating treatment outcomes, as well as the epidemiological impact of the programme. Important factors include:

- ensuring that training, supervision, logistics and communication activities are being carried out effectively at each level from the national level to the peripheral clinic;
- deciding whether health units are collecting the data needed to assess case notification rates and treatment outcomes;
- identifying technical and operational problems, specifying the reasons for the problems and taking the necessary corrective actions;
- assisting staff to improve standards of practice;
- improving patient care and support, and the quality of information.

18.1 Indicators

The use of indicators provides a convenient way of measuring programme performance, including the coverage targets (monitoring), reaching strategic and outcome objectives (evaluation) and impact objectives (epidemiological surveillance).

Routine reporting, described in Chapter 3, provides the data to calculate most of the indicators. A useful indicator should be easy to measure, provide a valid measure of the

relevant factor, be reproducible, give the same result when measured by different people in similar settings and be comparable across settings. A few performance and impact indicators, based on routine data, are usually sufficient. Additional indicators may be used in special studies to detect and address problems. Examples of monitoring and evaluation indicators are given in the Stop TB Planning Matrix.[1]

18.2 Cohort analysis

Cohort analysis is the key management tool used to evaluate the effectiveness of TB control activities in any given area. It may be used to identify the quarterly and annual treatment success rates (percentage of patients who are cured plus those who complete treatment) and provide middle- or higher-level managers with timely, concrete indicators of achievement. The quarterly smear conversion report and treatment outcomes enable the identification of problems, so that appropriate action may be taken to improve programme performance (e.g. low cure rate, high default rate, higher than expected proportion of sputum smear-negative PTB or extrapulmonary TB, and lower than expected case detection rate).

18.3 Measurement of impact

The establishment of targets within the MDG framework, and of subsequent targets developed by the Stop TB Partnership, have provided greater impetus in the evaluation of TB programmes. NTPs need to measure more actively the epidemiological impact of TB control, in addition to monitoring implementation of the Stop TB strategy. The evaluation

[1] http://www.who.int/tb/dots/planningframeworks/gf_tb_proposals_preparation/en/index.html

of the impact of TB control requires the measurement of TB prevalence, incidence and mortality.

18.4 Recording and reporting

The recording and reporting system allows for targeted, individualized follow-up to help patients who may not be making satisfactory progress, and for a rapid managerial assessment of the overall performance of each institution, district, region or country. This strong system of accountability and cross-checks avoids false reporting of data.

Evaluation of treatment outcome takes place about three months after all patients in the cohort have completed their course of treatment.

The steps involved are:

- cohort analysis of treatment outcome by the district TB officer every quarter and at the end of every year;
- district quarterly reports on treatment outcome forwarded to the intermediate level (e.g. region) for verification;
- verification that district reports are correct, complete, dated, signed and consistent; compilation of cohort analysis reports on all patients in the region;
- submission of the report to the central unit of the NTP;
- compilation of cohort analysis reports on all TB patients registered nationally.

18.5 Global information system

WHO has established a global information system to evaluate progress in implementing the six components of the Stop TB strategy, assess the quality of DOTS through treatment outcomes, and estimate TB morbidity. A TB data collection form, which changes slightly from year to year to accommodate global needs in monitoring approaches to TB control, is distributed to the national health authorities of all countries and territories. From the responses, WHO assesses progress in implementing the six components of the Stop TB strategy and results, compared with the global targets. Case reporting is measured against the estimated TB incidence in each country. The data and conclusions are published annually.[1]

WHO guidelines

Guidelines for conducting a review of a national tuberculosis control programme. Geneva, World Health Organization, 1998 (WHO/TB/98.240; available at http://www.who.int/tb/en).

Treatment of tuberculosis: guidelines for national programmes, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

Key references

Assessing tuberculosis prevalence through population-based surveys. Manila, WHO Office for the Western Pacific, 2007 (available at http://www.wpro.who.int/NR/rdonlyres/F49273CB-4CAB-4C38-B1E3-500108BA4A97/0/AssessingTBprevalence.pdf).

[1] Further information about WHO's monitoring activities, global information and reports is available at www.who.int/tb or by e-mail request to cdsdoc@who.int.

Compendium of indicators for monitoring and evaluating national tuberculosis programmes. Geneva, World Health Organization, 2004 (WHO/HTM/TB/2004.344)

Enarson DA et al. *Management of tuberculosis: a guide for low income countries*, 5th ed. Paris, International Union Against Tuberculosis and Lung Disease, 2000.

Global tuberculosis control: surveillance, planning, financing. WHO report 2007. Geneva, World Health Organization, 2007 (WHO/HTM/TB/2007.376; available at: http://www.who.int/tb/publications/2007/en/).

Chapter 19 Funding of tuberculosis control

Country-level planning and budgeting for TB control that are in line with the Stop TB Strategy and the Global Plan to Stop TB are essential for achieving the MDG and Stop TB Partnership targets set for 2015. Resource mobilization from national governments and donor agencies to ensure that these plans are fully funded is also essential.

Many NTPs operate under severe financial constraints and have to compete with other health programmes for budget allocations from the government and donors. Rationalization of the allocation process can be influenced by the use of economic analysis, such as cost-effectiveness analyses. Familiarity with the main types of economic analysis, how they are undertaken and how they may be used to convince policy-makers about the relative benefits of investing in TB control is therefore important.

19.1 Budget planning

The development of budgets for medium-term strategic plans and one-year operational plans should be a core component of TB programme management in both centralized and decentralized systems, and is a key task for national and subnational TB programme managers in particular. Budgeting should ensure that the funds needed for all programme inputs and activities are accurately identified, and included in a budget request for the TB programme specifically and/or as part of general district budgets for health care. Ideally, this should be done for each major component and subcomponent of the TB control programme

separately, as well as for all components combined. Any investment required in general health services for TB control should also be identified.

Once the budget has been finalized, a clear picture of the funding available from the government and donor agencies should be developed. This is necessary to define where funding gaps exist and where further resource mobilization is needed. A clear understanding of funding needs and where funding gaps exist is fundamental to effective programme management and, in particular, for negotiations about funding with national or local authorities, closely-related programmes or initiatives (e.g. HIV/AIDS programmes or the PEPFAR[1] initiative), and donor agencies.

19.2 TB planning and budgeting tool

To assist in the assessment of funding needs as well as the subsequent tracking of funding and expenditures, WHO has developed a planning and budgeting tool for use by NTPs.[2] It is designed to help countries develop plans and budgets for TB control at national and subnational levels within the framework provided by the Stop TB Strategy and the Global Plan to Stop TB, and to identify the available funding and funding gaps that remain to be filled. These plans and budgets allow routine monitoring of TB control and provide the basis for resource mobilization.

[1] President's Emergency Plan for AIDS Relief, launched by President Bush. Funding has amounted to US$ 15 billion during the five years 2003–2008.
[2] http://www.who.int/tb/dots/planning_budgeting_tool/en/index.html

The tool is an Excel-based spreadsheet in which plans and budgets for all major components of the Stop TB Strategy may be developed. Accompanying documents and related links are available to help users to understand and use the tool effectively.

Some of the key features of the tool are:

- It is Excel-based with an inbuilt user guide and menu system for navigating between worksheets and within worksheets.
- There is one worksheet for each major component of TB control.
- Each worksheet allows for detailed development of plans and budgets, or for the calculation of “quick estimates”.
- Each worksheet includes a ready-made list of likely inputs and activities to consider as well as default values.
- The tool is flexible, e.g. names of inputs and activities and default values may be modified as appropriate.
- An “application options” feature is included to enhance user-friendliness.
- It includes historical, epidemiological, demographic and financial data and epidemiological/demographic projections up to 2015.
- It is designed to assist with projections of key indicators that underpin any plan and budget, e.g. the number of patients to be treated.
- There is a status bar to show the status of work done within the tool.
- Summary tables and figures are automatically produced, including the financial information requested annually by WHO and summary budgets required for

proposals to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund).

Use of the tool offers a number of advantages, including:

- It can save time and improve the quality of plans and budgets.
- Plans/budgets may be easily revised or updated.
- Much of the plan document may be produced by writing a description of what has been set out in the tool.
- Plans and budgets for TB control are set out comprehensively in one place.
- Standardized presentation facilitates comparisons between and within countries.
- It facilitates analysis of financial gaps and preparation of a detailed budget in accordance with Global Fund requirements.
- It provides a framework for monitoring and evaluation of TB control, including of Global Fund grant implementation and expenditures.

19.3 Sources of funds for TB control

Funding for TB control may be divided into two major types: domestic and donor funding.

19.3.1 Domestic funding

Domestic funding comes from national governments as well as from local governments or authorities at lower administrative levels (e.g. provinces, districts) in decentralized systems. Funds may be raised from tax revenues, social or private insurance schemes, and

out-of-pocket expenditures. Loans from external sources such as the World Bank also qualify as domestic funding. Overall, across the 22 high TB-burden countries, about 70% of the total funding for TB control was provided by domestic sources (including loans) in 2007, although there is considerable variation among these countries (from 12% to 97% in 2007).

19.3.2 Donor financing

Donor financing comes from two major sources: the Global Fund and bilateral donor agencies.

Domestic funding from national and local governments should provide the foundation for the funding of TB control, and the share of total funding needs that is covered from domestic government sources is a key indicator of political commitment. Donor funding is often less reliable and predictable, may never or only rarely cover certain key inputs to TB control (e.g. staff and health systems infrastructure, though there are recent exceptions such as the PEPFAR initiative) and long-term commitments (e.g. for the five years of a strategic plan) may be hard to achieve. Moreover, too much dependence on external funding may leave an NTP vulnerable to shifts in donor priorities. As a general benchmark, the Commission on Macroeconomics and Health indicated that middle-income countries should have the capacity to fund most or all of their health care (including TB control activities) from domestic sources, and that low-income countries might provide around 90% of their health-care funding requirements. The least developed countries, which are mainly in Africa, would, however, need donor funding to cover about 50% of their funding needs.

The share of total government health expenditures that are required for TB control may be assessed by comparing funding requirements for TB control with national health account data.[1] NHA are used to assess all expenditures on health care, by source of funding, and are available online.

19.3.3 Global Fund to Fight AIDS, Tuberculosis and Malaria

As of 2007 the Global Fund had become the largest source of donor funding for TB control in the world today. It issues regular calls for proposals, and countries with well-planned proposals have been successful in filling many of their financial gaps for TB control

WHO provides a planning matrix for proposals to the Global Fund in line with the Stop TB Strategy delivery areas, including possible indicators and budget items. This is accompanied by planning frameworks giving more detail on possible activities based on current guidelines. The matrix and planning frameworks are consistent with the TB planning and budgeting tool. The planning and budgeting tool facilitates analysis of financial gaps and preparation of a detailed budget in accordance with Global Fund requirements. It may also facilitate the monitoring of Global Fund grant expenditures.

[1] www.who.int/nha

19.3.4 PEPFAR

Presidential Emergency Plan for AIDS Relief (PEPFAR) launched by the US government in 2003 has provided substantial new donor funding for interventions related to HIV/AIDS prevention, treatment and care. Most of the funding has been for 14 African countries, and in these countries PEPFAR offers a major opportunity for increasing funding for some components of TB control, including collaborative TB/HIV activities and strengthening of laboratory infrastructure.

WHO guidelines

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Report of the Commission on Macroeconomics and Health. Geneva, World Health Organization, 2001.

Links for further information

Global Fund to Fight AIDS, Tuberculosis and Malaria: http://www.theglobalfund.org/

Stop TB Partnership/Global Plan: http://www.stoptb.org/globalplan/

Stop TB Department: http://www.who.int/tb/strategy/en/

Stop TB Department. Global Fund proposal preparation: http://www.who.int/tb/dots/planningframeworks/en/index.html

World Health Organization. National health accounts, 2007: www.who.int/nha

Chapter 20 Legal and regulatory issues

Measures to control TB should be carried out in compliance with international and national legislation and regulations pertaining to communicable diseases, and specific provisions concerning TB. NTPs should be aware of the provisions applicable to TB. The following sections outline the main categories of legal and regulatory measures that are relevant to TB control.

20.1 International Health Regulations (IHR) 2005

The purpose of the IHR (2005), which entered into force in June 2007, is "to prevent, protect against, control and provide public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade". The mandate is much broader than that of the previous IHR (1969) in which the provisions applied primarily to plague, cholera and yellow fever. The IHR (2005) provide generally for any event with the potential to cause a public health emergency of international concern, which may be of biological, chemical or radionuclear origin, and whether or not the etiology is known at the time. Provisions include (i) routine public health measures at ports, airports and ground crossings and (ii) identification of and response to public health emergencies.

Notification of TB to WHO is not required under the IHR (2005) unless a potential international emergency is involved. Situations in which TB may potentially fall within the scope of the IHR might arise in connection with international travel by infectious TB patients,

particularly those with MDR-TB or XDR-TB. The IHR (2005) include a Decision Instrument, with criteria to identify events that are to be notified (Article 6; Annex 2).

When WHO is informed of an event that might potentially represent an international public health emergency, a consultative process of risk assessment take place with the national health authority on the risks posed and any further measures to be taken (Articles 6–13) . Subject to various protections, States Parties may require: (i) international travellers to provide information on the itinerary and review of travel documents; (ii) non-invasive medical examinations (that could include sputum examination) to determine whether or not a public health risk is involved; and (iii) additional procedures, depending on evidence and circumstances (Article 23).

Provisions are included in the IHR (2005) to protect international travellers against unjustified health measures and to respect their human rights; these cover informed consent for medical examination and health measures, confidentiality of personal data, and protection against charges for health measures applied for public health protection.

States Parties have, as a requirement, a national IHR focal point at central level (usually in the ministry of health). In the case of a TB event involving the IHR, the WHO country and regional advisers for TB and the NTP manager will be the points of contact for the national IHR focal point during investigation and follow-up.

20.2 National communicable disease legislation

Legislation on communicable disease control is an essential expression of national political commitment. Regulations based on that legislation are adopted to apply its principles and provisions, including those concerning TB. The NTP manager is required to be informed about and comply with the pertinent national legislation and regulations. National communicable disease legislation is being revised in many countries to align it with obligations under the IHR (2005).

In countries where adequate health legislation does not exist, the NTP should advocate for its adoption. Legislation, through general provisions, should empower the ministry of health to produce health regulations, including regulations for TB control. Such regulations may be modified and updated according to changes in epidemiology or technical resources (whereas national legislation is less readily revised).

The purpose of legislation is to support the prevention and control of TB while protecting public health and the legal rights of individuals. A WHO “good practice” model for communicable disease legislation and TB regulation is available. It is recommended that national TB control regulations should include measures for:

- protecting uninfected individuals against *M. tuberculosis* infection;
- detecting TB cases and initiating anti-TB treatment at an early stage;
- adequately treating all patients with active TB;
- minimizing the misuse of anti-TB medicines;
- notifying and reporting TB cases;

- screening close contacts of TB patients;
- making BCG vaccination available for all eligible children;
- providing prophylactic treatment for certain groups of infected people (e.g. PLHIV);
- ensuring access to HIV prevention, care and treatment in higher HIV-prevalence settings.

Legislation should respect human dignity and rights as well as public health. However, legislation should make provision for certain extraordinary situations where involuntary

> Where voluntary compliance cannot be obtained, compulsion should always be regarded as the action of last resort and applied with safeguards to ensure that it is fully justified, strictly provided by the law, non-discriminatory, with possibility of appeal, of limited duration, subject to review and that the least restrictive option is applied. Compulsory measures should be commensurate with the resulting benefit and applied in the expectation that effective action will result.

compliance with key measures is required to protect public health, subject to appropriate safeguards (e.g. mandatory medical examinations, isolation, quarantine) or where other measures such as contact tracing may be necessary.

Measures applied to international travellers will also need to accord with the country's obligations under the IHR (2005).

20.3 National legislation and regulation of pharmaceutical products

A legislative framework is in place in most countries to implement and enforce a national drug policy and to regulate the activities of both the public and private sectors. However, the

framework for drug regulation varies from country to country, and in some it is very limited in scope and application. NTP managers should be aware of the existing national legal provisions concerning anti-TB medicines and how they are applied.

The national drug regulatory authority develops and implements most of the legislation and regulations on pharmaceutical products. Its responsibilities include registration of drugs; controls on imports and marketing; licensing; inspection and enforcement; monitoring of adverse drug reactions; and quality control.

20.3.1 Drug registration

An important task of the drug regulatory authority is to institute a system that subjects all pharmaceutical products to premarketing evaluation and marketing authorization, also known as *drug registration*, to ensure that products conform to required standards of quality, safety and efficacy. Drug evaluation and registration include the review and approval of the product data sheets and labels. This information is usually disseminated through drug inserts or drug formularies.

20.3.2 Import and market controls

The marketing surveillance activities of the drug regulatory authority integrate administrative procedures to ensure that pharmaceutical products are imported only if they have received an import licence before reaching the country. The entity responsible for importation of pharmaceutical products should comply with all specifications on the relevant import licence. All imported products should have been registered by the national drug regulatory authority

or should have received a marketing authorization. Exceptionally, a waiver may be granted based on public health considerations.

20.3.3 Licensing

A mandatory system of licensing manufacturers, importing and exporting agents, distributors and retail pharmacies is usually in place to ensure that all products conform to acceptable standards of quality, safety and efficacy. In addition, all premises and practices used to manufacture, store, distribute and dispense these products should comply with requirements to ensure continued conformity to standards until products are delivered to the end-user. Overall quality assurance of drug manufacture is essential to ensure good quality. These practices are defined in good manufacturing practice (GMP) guidelines. The entity involved in the importation, exportation and distribution chain should ensure the proper storage of products, and their appropriate handling, packaging and distribution. These practices are defined in good distribution practice (GDP) guidelines.

20.3.4 Inspection and enforcement

Inspection is an important strategy for safeguarding drug quality. It is intended to ensure that all activities in drug manufacture, import, export, distribution, etc. comply with regulatory and quality assurance requirements, as well as with regulations. The drug regulatory authority usually establishes its own enforcement strategies to promote compliance with drug regulations. The strategy should be based on a pyramid of sanctions to be applied in a proportionate manner in cases of non-compliance.

20.3.5 Monitoring of adverse drug reactions

National pharmacovigilance systems collect and evaluate information on adverse drug reactions. Some countries have established their own adverse reaction reporting mechanism, and the regulatory capacity to use the information gathered. Examples of possible actions include suspension of a drug's market approval, the recall of certain batches, a warning in a national drug bulletin or a separate warning sent out to a list of institutions and main prescribers.

20.3.6 Quality control

Drug quality control laboratories are responsible for checking, by appropriate testing, whether drugs are of the required quality. Each drug regulatory authority should have access to a quality control laboratory, which will also play an important role in the registration process and in the surveillance of the quality of marketed products. For relatively small countries, quality control may be coordinated at a regional centre.

20.4 Occupational health legislation.

The WHO *Declaration on occupational health for all* (1994) calls upon governments to prepare a special national policy and programme for occupational health, including provision of competent occupational health services for all people at work. Such a programme should include the development of appropriate legal provisions, and systems for enforcement, with inspection by competent occupational health authorities. The Declaration specifies the characteristics of a well-organized and competent occupational health service.

The NTP should be aware of the existing national legislation and regulations concerning occupational health. In health-care settings, medical and other staff may be at significant risk of exposure to *M. tuberculosis* infection (see Chapter 6). In the event of infection occurring among staff, legal action may be envisaged by the infected staff if adequate measures to prevent transmission of *M. tuberculosis* have not been implemented. Staff should be fully informed of the national occupational regulations and any possibilities that exist for compensation in the event of infection acquired in the workplace.

20.5 International regulations on transport of infectious substances

Recommendations on the transport of infectious substances are included in the Model Regulations on the Transport of Dangerous Goods, developed by the United Nations Economic and Social Council's Committee of Experts on the Transport of Dangerous Goods and updated every two years. These recommendations form the basis of national and international transport regulations. Packing requirements, labelling and documentation are subject to regulation for the national (where applicable) and international transport of infectious substances.

For the international transport of TB samples, cultures of *M. tuberculosis* should be shipped according to United Nations packaging instruction P620 and accompanied by the appropriate dangerous goods documentation (shipping declaration UN2814).

Other TB-containing specimens should be shipped according to United Nations packaging instruction P650. No accompanying dangerous goods documentation is required in these cases (shipping declaration UN3373).

Laboratories that send TB samples should be aware of all applicable regulations and have the necessary materials available. It is advisable to identify locally available services and have supplies and local arrangements in place in advance.

Key references

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Laboratory biosafety manual, 3rd ed. Geneva, World Health Organization, 2004.

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Quality assurance of pharmaceuticals: a compendium of guidelines and related materials. Volume II. Good manufacturing practices and inspection. Geneva, World Health Organization, 2003.

WHO Expert Committee on specifications for pharmaceutical preparations. Fortieth report. Geneva, World Health Organization, 2006 (WHO Technical Report Series No. 937; Annex 5: Good distribution practices for pharmaceutical products).

Part III Ensuring comprehensive control of tuberculosis

The Stop TB Strategy, launched in 2006, is based on a comprehensive approach to TB control which recognizes the importance of many factors that go beyond the essential elements of the DOTS strategy. These factors reflect the need to integrate and involve TB control in the broader context of health systems and health system reform; to engage all health care providers and involve communities, and to pursue an equal access to TB services for the entire population, particularly the most vulnerable groups. The TB control programme should also be involved in research so that the development of new tools is encouraged in accordance with programme needs, and the introduction of new tools is facilitated. This section focuses on the subject areas which extend the scope of activities of the NTP as needed to ensure comprehensive TB control. To implement the Stop TB Strategy, these activities should be integral elements in the NTP and not viewed as optional extras.

Chapter 21 Contributing to strengthening of health systems

The NTP functions within, and is an important part of, the national health system. It is consequently involved in, and affected by, the functioning of the system and any health sector reform initiatives. It is important for the NTP, together with other public health programmes, to play a constructive role in strengthening health systems, to ensure that TB control brings benefits for the general health system and to ensure that TB services are not disadvantaged as a result of reform measures.

21.1 Analysing barriers to health system strengthening

Through analysis of health systems barriers to TB control, the NTP may help increase understanding of the root causes of weak health systems, such as weak governance, inadequate health financing, an insufficient work force and uncoordinated service delivery. Box 21.1 provides a list of potential health systems barriers to effective TB control, grouped according to the six health system building blocks defined in WHO's framework for action on health system strengthening. The NTP is often well equipped, through its use of a standardized monitoring and evaluation system, to provide concrete and specific information that may help improve understanding of general health system weaknesses. For example, the routine monitoring of performance indicators, such as trends in the number of TB suspects investigated in relation to the number of outpatient visits in general health facilities, trends of rates of sputum smear positivity, case notification trends and trends in treatment outcomes, provides information about the overall health system within which the NTP operates. Similarly, monitoring of programme management, including health workforce, drug

management, laboratory quality, role of private sector and community, may help identify areas of the general health system in need of improvement. These observations should be shared with relevant partners involved in strengthening of the general health system.

BOX 21.1

POTENTIAL WEAKNESSES OF HEALTH SYSTEMS, AND IMPLICATIONS FOR TB CONTROL

Leadership and governance (stewardship)

- Weak capacity for health policy analysis, priority setting, sector policy development and central health sector management. This may involve both quantitative and qualitative manpower limitations as well as limitations related to planning and decision making structures.
- Poor coordination between different public sector entities involved in health care planning and implementation, including limited coordination between different ministries and between national, provincial, city corporation and local governments.
- Decentralization with increased local autonomy without sufficient legislation and central coordination securing adequate disease control measures.
- Weak health sector regulation and limited mechanisms and resources for enforcing existing regulation
- Non-existent or weak policy concerning the role of the private health care sector, including limited information on the private sector and poor regulatory framework

Health financing

- Limited general health sector budgets and caps on expansion of health resources
- Unfair financing systems, e.g. absence or low coverage of health insurance with ability to pool and redistribute resources in a way which minimizes financial access barriers
- Weak financial steering mechanisms for strategic resource allocation and purchasing of services
- Weak mechanisms for tracking financial flows and poor capacity for performing national health accounts

Health workforce

- Lack of basic information about the health work force density, distribution and skill mix
- Insufficient size and competence of the health workforce.
- Weak structure and poor quality of educational systems for health professionals.
- Weak structure and quality for continued medical education
- Absent, unclear or non-performance based career opportunities
- Poor supervision and quality control mechanisms
- Perverse incentives linked to employment policies, salary structure and payment mechanisms

Medical products (including drugs and diagnostic facilities)

- Weak regulation of medical products and/or weak enforcement mechanisms
- Weak mechanism for promoting rational use of drugs
- Weak systems for procurement, distribution and management of drugs and equipment

Health information system (including monitoring and evaluation)

- Poor quality of vital statistics and demographic information
- Weak general systems for disease surveillance, and poor disease notification system
- Lack of data on health care utilization patterns
- Limited skills to analyse existing data
- Limited capacity for health systems research and operational research

Health services (including health care provision and management/ supervision of services)

- Lack of basic information concerning number, composition, and geographical distribution of all health providers (public and private), and the type and quality of the services they provide
- Lack of comprehensive policy and plan for optimal utilization of existing health providers
- Limited capacity to plan and manage health care provision, including contracting, certification and accreditation of public and private providers
- Limited use of quality standards and evidence based guidelines
- Poor systems for referrals and information exchange between providers

21.2 Identifying opportunities and threats in processes for health sector development

Health sector reforms can bring major opportunities for improved TB control, through improving health-care financing, infrastructure, health workforce capacity, etc. However, health sector reforms are shaped through complex political processes. NTP managers are not usually at the centre of such processes, and may not be fully informed about them. Consequently, TB programmes may be at risk of being neglected or even damaged during health sector reforms, and opportunities for TB programmes to contribute to general health systems strengthening may be lost.

NTPs need to stay in touch with, and seek to influence, health sector reform processes. Reforms that may be implemented include decentralization and devolution of health care financing and decision-making; privatization and/or provider–purchaser split with more independent health institutions; and changing financing mechanisms, e.g. introduction of health insurance schemes.

NTPs also need to be informed about broader health-care planning and financing frameworks, processes and concepts that are used by ministries of health, partners and international donors. These include sector-wide approaches (SWAPs), medium-term expenditure frameworks (MTEFs) and poverty reduction strategy papers (PRSPs).

21.3 Contributing to system-wide solutions while protecting essential TB control functions

Having identified health system barriers and mapped out ongoing and planned health sector development processes, NTPs should devise actions to strengthen health systems that:

- contribute to addressing the root causes of health system weaknesses;
- optimize the positive impact on the general health system of specific TB programme activities, through appropriate integration and harmonization of financing, planning and service delivery;
- protect essential TB-specific functions that may be damaged during health sector reform processes.

The NTPs should, to the extent possible, be proactively involved in national health sector development processes. The opportunities for the NTP to directly influence broad reform processes vary from country to country. Often, the NTP will be able to address general health systems barriers only indirectly through its own operations. However, this can also be an important leverage point. For example, when the NTP addresses health system barriers on a daily basis, by trying to secure sustainable funding, striving to improve the workforce and laboratory capacity, optimizing drug management and improving coordination between different health-care providers, these efforts will help strengthen the general health system, provided that they are harmonized with national health plans, with the aim of optimal use of shared resources.

Although disease-specific investments in, for example, HR development or laboratory strengthening, may help improve the general health system, they may also put strain on the health system and drain resources from other parts of the system if planned and implemented in isolation without due consideration of system-wide effects. Contributing to health system strengthening implies a responsibility to consider the impact of TB control actions on the wider health system. Therefore, the NTPs should promote:

- *harmonizing* TB control planning and budgeting processes with sector-wide planning frameworks;
- *optimizing* the use of shared resources, such as frontline health staff;
- *reducing* the number of duplicative structures.

Harmonization and integration should not compromise core TB control functions. The key functions normally require sufficient earmarked resources and dedicated staff for programme units at central and regional/provincial levels, dedicated staff for programme supervision at district level, and, unless the general health system is strong enough on these functions, separate reporting of key programme indicators and capacity to manage procurement and distribution of anti-TB drugs. The balance between integration and the retention of key TB-specific structures and staff will vary across countries, depending on the robustness of the general health system.

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Chapter 22 Engaging all care providers

The delivery of care for TB patients through public sector health services is generally the main focus of NTP activities. However, many patients with symptoms of TB, including very poor patients, seek and receive care from a wide variety of private and public health-care providers outside the network of NTP services. The involvement of these non-NTP providers varies greatly from country to country. The systematic involvement of all relevant health-care providers in delivering effective services for diagnosis of TB and treatment of TB patients to all segments of the population is an essential component of the Stop TB Strategy. Table 22.1 lists the major provider groups that may manage TB patients outside the NTP.

TABLE 22.1 CATEGORIES OF HEALTH CARE PROVIDERS THAT MANAGE TUBERCULOSIS PATIENTS

Public health-care providers	Non-state or private health-care providers
General hospitals	Private hospitals and clinics
Specialty hospitals and medical colleges	Corporate health services
Health institutions under state insurance schemes	Nongovernmental organization hospitals and clinics
	Faith-based organization services
Health facilities under public corporations	Individual private practitioners
Prison health services	Pharmacies and drug dispensaries
Military health services	Traditional healers and practitioners
	Informal, non-qualified practitioners

22.1 Public–private mix

The term “public–private mix”, or PPM, represents a comprehensive approach for engaging all relevant health-care providers in care of TB patients and control of the disease. It encompasses all forms of public–private collaboration (e.g. between NTP and the private or

corporate sector), public–public collaboration (e.g. between NTP and hospital or prison health services) and private–private collaboration (e.g. between an NGO or a private hospital and the neighbourhood private practitioners) for the common purpose of ensuring provision of standard TB care in the community. PPM is also relevant for laboratory work, TB/HIV collaborative activities and for prevention and management of drug-resistant TB, including MDR-TB and XDR-TB.

The *International standards for tuberculosis care* address the basic elements of diagnosis of TB and treatment of TB patients and provide an excellent tool to help standardize TB management practices among all care providers.

22.2 Implementing public–private mix at national level

Evidence from country experiences shows that PPM for TB care and control is feasible, productive and cost-effective: it helps to improve TB case detection and treatment outcomes, it fosters equity of access to TB care, and it affords financial protection for the poor.

The standard country-level PPM approach involves three main activities:

- undertaking a national situation assessment;
- developing national operational guidelines and plans;
- implementing guidelines and plans locally.

22.2.1 National situation assessment

The steps involved in a situation assessment include:

- identifying all health-care provider groups;
- determining their current contribution to TB control;
- assessing which TB control tasks each provider group can undertake;
- identifying input required from NTPs to optimize their contribution.

A generic tool to help countries undertake a national situation assessment is available. Table 22.2 provides some options for task mix and role division for different types of providers, which will vary across and within countries depending on the nature of provider mix, willingness to take on different tasks, the status of the NTP, patient preferences and the health regulatory framework.

TABLE 22.2 INDICATIVE TASK MIX FOR DIFFERENT CATEGORIES OF HEALTH-CARE PROVIDER[a]

	Tasks	National TB control programme	Public or private institution	Individual private provider	Private/ public laboratory	Non-physician/ pharmacy
Clinical tasks	Identify symptomatic TB patients	■	■	■	■	■
	Collect sputum smear samples	■	■	■	■	■
	Refer TB suspects	■	■	■	■	■
	Notify/record cases	■	■	■	■	■
	Supervise treatment	■	■	■	■	■
	Do sputum smear microscopy	■	■	■	■	
	Diagnose TB	■	■	■		
	Prescribe treatment	■	■	■		
	Inform patients about TB	■	■	■		
Public health tasks	Identify and supervise treatment supporters	■	■			
	Follow up defaulters	■	■			
	Train health-care providers	■	■			
	Supervise	■	■			
	Assure quality of laboratories	■	■			
	Monitor and evaluate	■	■			
	Manage drugs and supplies	■				
	Provide stewardship: financing and regulation	■				

[a] Shaded cells represent tasks that could be carried out by respective provider type.

The NTP should be able to carry out all of the tasks and to fill the gaps by supporting or taking on the tasks that other providers are unwilling or unable to carry out. In all settings, it is essential that the NTP is responsible for covering the main part of the cost of diagnosis and treatment. As a minimum, the NTP should provide anti-TB drugs free of charge to providers,

who should dispense them free of charge to patients. The NTP should also develop and maintain strong stewardship capacity to guide and oversee private and public providers. In brief, the government-run NTP assumes the responsibility for funding, regulating and monitoring, while the day-to-day collaborative implementation activities may be carried out by the local unit of the NTP or by appropriate non-NTP providers.

In developing a national strategy for PPM, the NTP should constitute a task force, coalition or coordination committee with broad representation of stakeholders (Table 22.3). This body may act as an interface between the NTP and other providers. It may also advise the NTP in carrying out various tasks such as advocacy, sensitization, training, supervision, quality control, and monitoring and evaluation. In some settings, the issue of diagnosis of smear-negative and culture-negative forms of TB has been addressed effectively by establishing diagnostic committees comprising relevant local experts.

TABLE 22.3 STAKEHOLDERS IN PUBLIC–PRIVATE MIX FOR DOTS AT NATIONAL, PROVINCIAL AND LOCAL LEVELS

- Ministry of health, its departments and sub-national counterparts
- Other ministries, such as ministries of labour, the interior, defence
- Health insurance organizations
- Drug regulatory authorities
- Academic institutions
- Social welfare programmes for poor and marginalized people
- Professional organizations
- Hospital associations, pharmaceutical associations etc.
- National and international nongovernmental organizations involved in delivery of services for TB control
- Drug industry
- Consumer organizations

22.2.2 Developing operational guidelines

National policy and operational guidelines on PPM should be developed and implemented as an iterative process: policy, leading to preparation of operational guidelines to help phased

implementation, and the results of implementation feeding back into policy for any revision required.

Table 22.4 summarizes the seven essential components of developing operational guidelines for PPM.

TABLE 22.4 ESSENTIAL COMPONENTS OF DEVELOPING OPERATIONAL GUIDELINES FOR PUBLIC–PRIVATE MIX APPROACHES

Component	Summary
Formulating objectives	Examples: increase in case detection; improved treatment outcomes; improved access to diagnostic and treatment services for poor people and impoverished communities; reduced financial burden for patients.
Defining the task mix	Roles and responsibilities for different providers clearly defined, providing different options so that guidelines can be adapted locally.
Developing practical tools	Examples: laboratory request form; referral-for-treatment form; feedback or back-referral form; transfer form; laboratory register; TB register; TB treatment card.
Developing a training strategy	Training strategy to be based on the defined task mix, and target staff of the national TB control programme staff and providers involved
Certification or accreditation of providers	Criteria for certification and de-certification to be related to the specific task options, similarly for the public and private sectors. Certification may be informal initially and evolve into a formal, standardized procedure.
Developing incentives and enablers	Financial compensation may be necessary for providers who manage a large number of TB suspects and cases. However, private practitioners with few TB patients and voluntary organizations providing TB care may find in-kind, non-monetary incentives sufficient to enter into collaboration with the programme, e.g. access to anti-TB drugs, training and continuing education and microscopy services, all free of charge.
Drafting monitoring and evaluation plan	Monitoring and evaluation of the public–private mix process in relation to defined objectives is needed to enable stepwise adjustment of strategies and implementation plans.

22.3 Implementing public–private mix at local level

The national guidelines should be flexible enough to allow for local adaptation. The logical steps in local implementation are: preparation, mapping and first contact with providers, selection of providers, implementation proper, and advocacy and communication.

22.3.1 Preparation

A clear, written message from the senior NTP management on the importance and priority of PPM is the first prerequisite before local implementation begins. Operational guidelines should be made available. Draft sensitization and training materials should be ready for use. The implementation tools, including any new formats and adapted NTP registers and reports, should be available. NTP staff should be oriented about PPM; their tasks and responsibilities should be defined and a plan of implementation should be available according to locally defined objectives for PPM.

22.3.2 Mapping and first contact with provider

The local NTP unit should have a map of its area on which to mark all public and non-public providers. In dealing with private providers, using a neutral interface such as a local NGO or a civil society institution may expedite both provider enrolment and programme implementation. Mapping and making the first contact with the provider and sensitization may be combined.

22.3.3 Selection of providers

Prioritization of providers for active collaboration and their training are important steps. The following considerations should be taken into account.

- Institutional providers such as large hospitals and medical colleges are likely to give a higher yield of cases but will also require greater time and attention on the part of senior NTP staff.

- It may be possible to identify and target first the private practitioners who handle a large number of TB suspects and cases.
- Involving other public sector institutions within and outside the ministry of health may require a parallel process of approvals and directives from their senior regional or national managers.
- The poorest patients are likely to first approach NGOs operating in poor areas and non-physicians such as pharmacists, non-qualified providers and traditional healers. Approaching these categories may improve access for poor people.
- It is advisable to begin with willing providers before attempting to engage those reluctant to collaborate.
- Professional organizations and NGOs may serve as important intermediaries to enlist other care providers.

22.3.4 Implementation

The method of launching PPM locally will depend on the setting. It is important that NTP staff maintain their commitment and follow the agreed plans. In early stages, documentation of the process should be maintained. Careful monitoring and documentation of problems encountered are recommended so that appropriate revision of operational guidelines may be made. Continuous dialogue between involved partners is necessary to address identified problems and potential tensions.

22.3.5 Advocacy and communication

To generate and sustain interest in PPM, advocacy should be directed both towards NTP staff and their counterparts among other provider groups. All care providers are likely to benefit from improvement in their communication and interaction with TB suspects and cases. Providing information to patients on the availability of TB services in the public and private sectors and on the charges they may or may not need to pay for different services helps make the collaboration open and transparent and may also help to minimize the possibilities of misuse and malpractice.

22.4 Supervision and monitoring of PPM

Supervision and quality assurance of all involved public and private facilities, including laboratories, should be an integral part respectively of the supervisory and quality assurance routines of the NTP. Indicators for monitoring the process and measuring the contribution of providers to overall TB control targets include the following process and outcome indicators:

1. Proportion of reporting units implementing PPM.
2. Proportion of non-NTP health units participating in referral/diagnosis/treatment of TB cases.
3. Proportion of new smear-positive cases detected through referral by non-NTP providers.
4. Proportion of new smear-positive cases detected through diagnosis by non-NTP providers.

5. Proportion of new smear-positive TB patients receiving DOT from non-NTP providers.
6. Treatment outcomes of new smear-positive cases treated by non-NTP providers.

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Chapter 23 Practical approach to lung health and other integrated approaches to health care

The primary health-care concept is embodied in integrated, decentralized general health services that provide preventive measures as well as treatment and care for the community's most commonly occurring priority health problems. General health services offer valuable opportunities for the diagnosis and management of TB. Case detection, treatment and follow-up are enhanced when TB services are provided within the general health system at service delivery points. Facilitating factors include improved access to diagnostic and treatment services, reduction of stigma and simplified contact tracing. Several initiatives promote an integrated approach to priority health interventions.

23.1 Practical approach to lung health (PAL)

Respiratory conditions are the first or second leading cause of care-seeking in most primary health care (PHC) settings, accounting for some 20–30% of visits. Since TB accounts for only a very small proportion of all respiratory cases, TB suspects are often inappropriately managed and therefore TB is misdiagnosed. The PAL strategy addresses the need for improved respiratory care through a symptom-based integrated approach to the standardized management of patients with respiratory conditions in PHC settings. PAL emphasizes priority respiratory illnesses, particularly TB, acute respiratory infections and chronic respiratory diseases, with a focus on asthma and chronic obstructive pulmonary disease. Improving general respiratory care increases the quality of the identification of TB cases

among respiratory patients. This is the basic principle according to which the PAL strategy has been developed and incorporated in the Stop TB Strategy.

The IMCI initiative focuses on children aged below five years, including those with respiratory symptoms. PAL targets respiratory patients aged five years and over.

23.1.1 Key objectives

The PAL strategy focuses on the quality of management of patients with respiratory conditions among whom TB cases should be identified. It also defines how the management process should be adapted to the available health resources and infrastructure.

The two major objectives of PAL are:

- to improve the quality of respiratory care in PHC settings;
- to improve the efficiency of respiratory service delivery within health systems, focusing on the district health system.

23.1.2 Principal components

PAL includes two major components: standardization of clinical care and coordination within the health sector.

Standardization of clinical care. Clinical practice guidelines are needed for first-level health facilities and for referral levels; the two should be coordinated. First-level guidelines should

be symptom-based, while those for referral levels should deal with the specific respiratory conditions that are managed at this level.

PAL guidelines use a minimum number of key signs that lead to diagnostic classification, determination of degree of severity of disease and decision-making. The guidelines should be consistent with regulations on drug prescription and international recommendations on the management of priority respiratory diseases such as TB, pneumonia, asthma and chronic obstructive pulmonary disease. In country settings, the adapted PAL guidelines should be consistent with existing national guidelines for TB, HIV and other clinical guidelines such as those for the integrated management of adult and adolescent illness (IMAI).

Coordination within the health sector. In well-established PHC systems, coordination within the health sector implies organized collaboration among health workers at the same and different levels of the health system, and among different categories of health workers. For respiratory case management, the involvement of each health-care provider category and of each health-care level should be clearly defined so that full integration takes place within the health system, particularly at district level.

The development and implementation of the PAL strategy also requires coordination with national health resource planning and other priority national health programmes and PHC services.

23.1.3 Essential elements

The following essential technical and managerial elements should be considered in PAL development in all settings.

- *Essential technical elements*

a. Classification and diagnosis of cases through standardized, locally adapted guidelines for outpatient services.
b. Treatment using standardized regimens of proven efficacy and medicines included in the national list of essential medicines.
c. Minimum equipment for diagnosis and treatment of respiratory diseases defined for each level of the health service.
d. Health education of patients and their families on compliance, with treatment and preventive measures such as immunization, stopping smoking, avoiding triggering factors for asthma and reducing indoor air pollution.

- *Essential managerial elements*

a. Political commitment, as evidenced by decisions such as the designation of a department or officer responsible for PAL activities, the nomination of a national working group on PAL and the mobilization of funds to initiate activities.
b. Training health professionals in the use of PAL guidelines.

c. An ensured regular supply of quality-assured affordable drugs for managing respiratory diseases and the minimum equipment defined in the guidelines supplied to the health units
d. Utilization of the existing information system in order to provide minimum essential information for monitoring and evaluating PAL activities.
e. Pilot-testing of the technical and operational guidelines in areas representing average conditions of the health infrastructure of the country.
f. National plan for PAL implementation, taking into account the experience of the pilot area tested.

23.1.4 Adaptation and implementation

Adaptation of the PAL strategy at country level, according to the epidemiological and socioeconomic environment and prevailing national health policies and health priorities, should take into account the structure of the health system and the health resources available, particularly at district level. Adaptation involves the following elements.

- Adaptation starts with the establishment of a national working group on PAL to guide and support initial PAL activities. Assessment of the health environment is an important initial step in identifying the respiratory conditions to be included in the national PAL strategy and for adaptation of the guidelines to the existing health infrastructure and resources.

- PAL guidelines and training material should be developed and pilot-tested. They should cover priority respiratory illnesses, the equipment and essential medicines needed to manage them, the role of each health worker category, the process for referral, and the standardized information system for collecting data.

- A plan to implement PAL, either for specific regions or for the whole country, should be elaborated in close coordination with the NTP and the national PHC department, and in consultation with other relevant stakeholders. In country settings where the initiative of the Global Alliance against Chronic Respiratory Diseases has been introduced, the implementation of PAL should take into account the activities of this initiative.

- To scale up PAL implementation, financial support may be mobilized through the government and explored with bilateral and multilateral agencies involved in the development of health services within the country.

- PAL implementation should be under the leadership of a clearly identified coordination unit within the ministry of health, ensuring appropriate links with relevant services.

23.1.5 Benefits

Through standardization and coordination of respiratory care services, PAL offers opportunities for improved diagnosis and case management of priority respiratory diseases. The competency of health workers in PHC settings is enhanced through the use of evidence-based clinical guidelines, and cost savings accrue from reduction of inappropriate drug

prescription. PAL can contribute to integrating and strengthening health services within PHC and increasing the utilization of services by the population, particularly the socially disadvantaged groups.

23.2 Integrated disease management

The WHO initiatives IMAI (Integrated Management of Adolescent and Adult Illness) and IMCI (Integrated Management of Childhood Illness) both support the delivery of essential health services within the context of primary health care through simplified and standardized guidelines. The guidelines address the decentralization of essential services for priority health problems to the district hospital, health centre and community levels. They cover an integrated approach to prevention, care and treatment services, based on standardized protocols, training of staff and supportive supervision. Family-based care is promoted and human resource limitations are alleviated through "task-shifting" routine aspects of patient management and follow-up from doctors and medical officers to health workers, to community-based workers, and to the patients themselves (self-management). IMAI is a more recent and evolving initiative than IMCI on which it is modelled, and updated information is regularly provided on its web site.[1]

The IMAI and IMCI tools together address both acute and chronic HIV care and TB case detection, prevention of TB transmission; referral to and linkages with TB treatment are included in these tools. The IMAI *Acute care* guideline module expands from the PAL guidelines on cough or difficult breathing and fever to address all major acute syndromes. In

[1] Access all the IMAI tools, including training materials for the clinical guideline modules and district management tools, at http://www.who.int/hiv/pub/imai/en

addition, IMAI and the WHO Stop TB Department have jointly developed a new guideline module for first-level facility clinical teams, *TB care with TB-HIV co-management*. This guideline (and a short training course) addresses combined HIV and TB diagnosis, TB treatment combined with HIV chronic care, as well as TB/ART co-treatment. Management of patients with complicated TB/HIV is also addressed in the IMAI second-level learning programme for district hospital clinicians and in the clinical mentoring guidelines and training materials.[1]

The IMCI strategy is an integrated approach to child health that focuses on the overall well-being of the child. IMCI aims to reduce death, illness and disability and to promote improved growth and development among children aged under 5 years. IMCI includes both preventive and curative elements that are implemented by families and communities as well as by health facilities. The IMCI strategy promotes the accurate identification in health facilities of childhood illnesses in outpatient settings, ensures appropriate combined treatment of all major illnesses, strengthens the counselling of caregivers, and speeds up the referral of severely ill children. In the home setting, it promotes appropriate care-seeking behaviours, improved nutrition and preventive care, and the correct implementation of prescribed care. Children who present at the first-level health facility with cough of more than 21 days are referred to the referral facility for assessment of TB.

[1] The entire IMAI/IMCI toolkit including draft versions is accessible at http://www.who.int/hiv/capacity/Access_Sharepoint.pdf (registration required).

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Chapter 24 Equity of and access to services for prevention of tuberculosis and treatment of patients

The promotion of equity and access for all in disease prevention and control activities is based on the recognition of poverty as a major determinant of ill-health and a barrier to health care. There is a need to accelerate health progress in poor and socially excluded groups in order to reach the health-related MDGs and to reduce inequities in access to health care. The links between poverty and TB disease burden have been documented for many years. The incidence of TB is 20 times higher in low-income countries compared with that in high-income countries. This chapter highlights the population groups that are often not reached by routine TB control measures and outlines the practical approaches required to address their needs.

This section addresses the integration of pro-poor measures in NTPs and outlines the practical issues involved and options for action to improve access and minimize the financial burden for patients. The following six main steps are recommended.

Step 1. Identify the vulnerable groups in the country/region

- Assess the poor and vulnerable groups who face barriers to accessing both general health and TB services, which may include: those in absolute economic poverty; those disadvantaged by gender-related factors; marginalized ethnic groups; people living in remote locations; the urban poor; other people in special situations and groups.

- Establish a profile of poor people and vulnerable groups and their locations in the country/region using: government or other data on prevalence and distribution of poverty and vulnerable populations; any government documents on poverty reduction plans or strategies; information on which types of health-care providers are used by the poor; data from any local studies on socioeconomic status of TB patients and poverty-related disparities.

Step 2. Determine which barriers prevent access of vulnerable groups to TB services

- Identify the types of barriers that may exist in the country/region, including economic barriers, geographical barriers, social and cultural barriers, health system barriers.

- Determine, for each group, the main barriers involved in the country/region, such as: economic barriers (complexity of the pathway to care, costs to patients); geographical barriers (distance from and difficulty of journey to TB services); social and cultural barriers (stigma, gender-related factors, fear of losing work, lack of knowledge of TB and the available services); and health system barriers (lack of responsiveness to the needs of the poor, effects of decentralization on peripheral services).

Step 3. Assess potential actions to overcome the barriers to access

Identify and prioritize actions to address the following impediments to access.

- Economic barriers: integration of TB services in primary health care; encouragement of pro-poor, PPM initiatives; provision of TB diagnosis and treatment in the workplace; extension of microscopy services; avoidance of user fees; provision of

diagnosis and treatment free of charge; discouragement of unofficial charges to patients.

- Geographical barriers: extension of diagnostic and treatment services to remote, poor regions; bringing patients from remote areas to TB services; development of a community-based TB care model.

- Social and cultural barriers: promotion of community mobilization; ensuring that staff attitudes do not reinforce stigma; advocacy for worker protection to avoid loss of work as a result of TB; ensuring that the TB health promotion plan takes account of poor and vulnerable groups; ensuring that gender-related needs are addressed in TB control activities; exploring possibilities for referral mechanisms from traditional health-care providers.

- Health service barriers: modification of schedules for TB diagnostic and treatment services to meet local needs; developing the communication skills of staff; discouraging staff from discriminating against poor patients; using total quality management to ensure that services remain responsive to the needs of the poor; engaging in health service decentralization to promote capacity strengthening at the periphery and inclusion of TB control as a district-level priority.

Step 4. Review the situations and population groups requiring special consideration

- Identify the groups needing special consideration and their locations in the country/region, including: migrant populations (refugees, asylum seekers, economic migrants, displaced populations, cross-border populations); pockets of deprivation in wealthier countries (isolated ethnic minorities, homeless people and others); injecting drug users; prison populations (see Chapter 25).

- Decide upon actions to address the special needs of these groups: identify the specific needs of each of the groups; establish priorities for action based on needs, feasibility, available resources, effectiveness of the measures; examine current services available to the priority groups identified; define strategies to ensure the diagnosis, treatment and follow-up of TB cases for each targeted group; plan phased implementation of the pro-poor interventions selected.

Step 5. Explore possibilities for harnessing additional resources

- Assess: available strategies to engage in broad initiatives to improve access to health services; sources of funding for improvement of health outcomes; institutions offering additional financial and other resources for pro-poor measures in TB control programmes; human resources to expand the public and private sector involvement in TB services; and technologies to enhance efficiency and effectiveness of TB services.

- Facilitate access to additional resources by: engaging in broader poverty reduction or health sector plans; identifying potential new partnerships in the country; prioritizing

mechanisms offering greatest added value for increasing access to TB services; planning the preparation of funding proposals; involving other stakeholders in the planning process.

Step 6. Evaluate the impact of pro-poor measures

- Establish the basis for impact evaluation by setting specific targets for TB control in poor and vulnerable populations, assessing the distribution of TB in the population and poverty-related disparities among TB service beneficiaries.
- Facilitate the monitoring of poverty-related inequalities and the impact of pro-poor interventions by: identifying partners to carry out equity monitoring; including socioeconomic variables in routine data collection and analysis; including socioeconomic questions in TB prevalence surveys; conducting periodic studies of care-seeking; assessing who in the community benefits from TB services and who does not.

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Chapter 25 Special groups and situations

25.1 TB in prisons[1]

Prisons are effective incubators for TB, often associated with epidemic levels of active disease and high death rates, exacerbated by increasing rates of HIV infection among prisoners and a growing burden of MDR-TB. Documented rates of TB in prisons are usually 10- to 50-fold greater than concurrent rates in the civilian sector. TB control in prisons has therefore become a mainstream component of the global effort to expand DOTS.

25.1.1 TB transmission

TB in prisons is a public health concern not only for prisoners but also for prison staff, family members and the local community because of the opportunities for TB transmission between them. There are high turnover rates among prisoners on a yearly basis, and these prisoners return to their communities upon release. Visiting family members and prison health and security staff also represent important prison–community conduits.

25.1.2 TB control

Effective TB control in prisons requires the same components identified in the Stop TB Strategy. There are several specific issues to be addressed for the control of TB in this context.

[1] This section refers to prisons, jails and other detention centres.

- *Political commitment*. Political commitment, including that from prison and jail administrators, is critical for establishing appropriate conditions for diagnosis and treatment of TB in prisons and maintaining TB programme links that must cross the civilian and prison sectors.

- *Case holding*
  - The treatment of released prisoners on anti-TB therapy should be continued in the community with attention given to prisoner/family education and referral mechanisms.
  - TB patients who enter a detention system during a current course of medication should be rapidly identified so that adequate treatment may continue without interruption and the risk of acquiring drug resistance be avoided.

- *Active case-finding strategy*. Passive case detection through prison health facilities is inadequate because many persons enter prison with undiagnosed TB, and because conditions in jails and prisons are conducive to the rapid spread of disease. Therefore, it is essential that an active case-finding strategy be implemented in a prison TB programme, focusing on screening at entry into the system coupled with a strategy to detect respiratory symptomatic cases after entry. Investigation of dormitory or cell contacts may also be effective if prisoner collaboration is well-established.

- *Civilian-prison collaboration*. For a prison TB control programme to gain credibility and develop a sustainable system, effective civilian–prison links are essential. It is important that NTP staff respect their penal counterparts as equal partners and stakeholders. Also, the issues specific to the prison environment and the prison population should be recognized and addressed accordingly.

25.1.3 HIV control and prevention

TB is often the first disease presentation in HIV-positive individuals. HIV testing should be considered for those whose HIV status is unknown, following UNAIDS guidelines for testing, which include voluntary testing, pre- and post-test counselling and an assurance of confidentiality.

Strategies to prevent the spread of HIV in prisons should be implemented in accordance with UNAIDS recommendations. Measures include education programmes for staff and inmates, use of universal precautions, provision of medically supervised detoxification programmes for addicts, harm reduction programmes, and free confidential availability of condoms.

25.2 TB control in refugee and displaced populations

More than 85% of refugees originate from, and remain within, countries with a high incidence of TB. Refugees and displaced populations are at particularly high risk of developing TB. Crowded living conditions facilitate the transmission of TB infection, and susceptibility to TB disease is increased by coexistent illness, particularly HIV, and by poor nutritional status. TB is an increasingly important cause of morbidity and mortality among

refugee and displaced populations.

TB control activities may be implemented effectively and produce good treatment outcomes in appropriately chosen refugee and displaced population settings, and in post-conflict situations.

25.2.1 Acute phase

TB care and control are not priorities in the acute phase of an emergency when mortality rates are high owing to other conditions such as acute respiratory infections, diarrhoeal diseases, measles, malaria and malnutrition. The priorities during this phase are the provision of adequate food, water, shelter, sanitation, basic medicines and the control of common acute communicable diseases.

25.2.2 Initiating TB interventions

If TB is an important health problem, control activities should not be initiated until: (i) the death rate from all causes has been reduced to less than 1 per 10 000 population per day; (ii) basic needs for water, adequate food, shelter and sanitation are met; (iii) essential clinical services and basic drugs for common illnesses are available; and (iv) basic services are accessible to a large part of the population so that TB suspects can be identified and appropriate investigation and referral arranged.

TB control should be undertaken only if the security situation is sufficiently stable to enable implementation of activities and if no major movements of the camp or the population served

are anticipated in the near future. At a minimum, programme funding should be sufficient to enrol patients for 12 months and complete the treatment of all members of this cohort – a minimum of 18 months.

25.2.3 Role of the NTP

Whenever possible, the NTP of the host country should be involved in the development of the TB control activities for refugees and displaced people. The policies of the NTP in the country of origin should also be taken into consideration if refugees are likely to be repatriated. Coordination with UNHCR[1] in the planning stage is critical in order to minimize the risk of patients interrupting treatment when camps or populations are moved.

The priorities of TB control are first to identify and treat infectious patients with severe forms of the disease and those with smear-positive pulmonary TB. Once TB control activities are well established, it is appropriate to treat the other forms of TB, as resources permit.

TB control in this population setting should follow the principles of the Stop TB Strategy.

25.3 TB control and natural disasters

Natural disasters such as floods, typhoons, tsunamis or earthquakes may occur in areas where TB services are well organized. The health infrastructure may be damaged or destroyed, and health staff usually involved in TB control may be directly affected in these situations, resulting in interruption of TB control activities.

[1] Office of the United Nations High Commissioner for Refugees.

Patients who were on TB treatment in the disaster-affected areas may no longer have access to any appropriate drug distribution system. Many patients may be difficult to track for continuation of treatment and may therefore be lost to follow-up. Patients may receive inappropriate TB drug prescriptions from health-care providers outside the NTP. The NTP distribution system for anti-TB drugs and supplies is also likely to be disturbed in areas not directly affected by the disaster, where the existing health infrastructure may be overwhelmed by the additional urgent workload and redeployment of staff. The managerial activities of the NTP may be disrupted by assignment of staff to tasks related to the disaster situation and/or loss of staff due to the disaster.

To address such situations, the following actions should be considered.

- TB should be included in all rapid health assessments carried out in the acute phase following a disaster.

- Wide distribution of health education messages, targeting TB patients on the need to continue their treatment, through information channels accessible to patients in communities.

- The NTP should establish a list of health facilities able to ensure appropriate TB drug distribution to patients in the affected communities and in regions close to the affected area. These lists should be widely distributed in communities and among health-care providers of the region, including newly arrived NGOs/organizations.

- Restarting TB control activities under the leadership and coordination of the NTP in the affected areas and ensuring that adequate TB services are maintained in non-affected areas during the acute phase of an emergency.

- Training of and coordination with the NGOs/organizations involved in TB control should be ensured by the NTP.

- Ensuring the anti-TB drug supply to health facilities specified in the list established by the NTP.

- Distribution of the national TB control guidelines to organizations supporting health facilities involved in TB care and control in affected and non-affected areas.

- Control, by the national health authorities, of anti-TB drugs that might be provided through any new distribution system.

After the acute phase of an emergency, the following steps should be taken.

- Evaluation, by the NTP, of TB control activities carried out in the acute phase in affected and non-affected areas.

- Planning of implementation of TB control activities in the framework of the rehabilitation process in affected areas.

- Advocacy in order to maintain TB as a health priority at national level.

25.4 TB control in other special population groups

Several vulnerable minority population groups pose special challenges for TB control because of difficulty of access to services (see also Chapter 24). Barriers to access may be the result of economic, political, social, geographical or ethnic factors, and often more than one of these factors is involved. Depending on the country situation, these groups may include immigrants, seasonal migrant workers, refugees, asylum seekers, cross-boarder populations, nomadic populations, populations in remote areas, ethnic minorities, marginalized indigenous populations, homeless people and other vulnerable groups such as injecting drug users.

One or more of the “difficult-to-reach” population groups are present in most countries. Because they are generally not adequately covered by the routine TB services provided for the general population, the NTP should adapt and develop approaches to ensure that TB control services are available and accessible for these groups. The development and implementation of health interventions should involve social welfare institutions, NGOs and other professionals who are in contact with the groups concerned.

Each group needs to be carefully defined and located. Its health priorities should be identified and the access to health services assessed. The health care providers who usually work with these groups should be identified and involved in provision of TB control services. Strategies and measures to implement and improve TB care and control should be defined in

collaboration with these health care providers, social services and local NGOs. The interventions should be monitored and evaluated.

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Chapter 26 Involvement of communities and patients in tuberculosis care and prevention

Since the 1978 Alma Ata Declaration, the participation of people in, and their contribution to, the development of health systems has been recognized as central to primary health care and accepted as an essential element of many public health interventions. The health reforms of the 1990s have given somewhat less attention to community participation and social values in health system development, focusing more on technical, economic and managerial factors.

The challenges posed by major epidemics such as HIV/AIDS, TB and malaria, and the role civil society has played in helping individuals and families to cope with them, have certainly contributed to make people and health policy-makers more aware of the essential and complementary role that communities can play in ensuring high-quality patient care.

Effective partnerships between health services and the community may facilitate access by bringing services to people's homes, and reducing the cost of care-seeking for patients and health services as well as the cost of workload for staff. Carefully designed community and/or patient involvement initiatives also facilitate patient and community empowerment. Through the involvement of local communities, education on relevant health issues and stimulation of change in health-related behaviour, communities become increasingly knowledgeable and self-reliant.

The empowerment of patients and communities requires knowledge of individual rights and responsibilities, the ability to exercise them at social and political levels, access to information and the ability to utilize knowledge and skills as needed. The *Patients' charter for tuberculosis care* (the Charter) sets out the rights and responsibilities of patients. The rights concern care, dignity, information, choice, confidence, justice, organization and security. The responsibilities cover sharing information, adherence to treatment, contributing to community health and showing solidarity.

The Charter identifies ways in which all stakeholders may work together in an open and positive relationship. While its basic principles are universal, cultural differences may influence the roles expected of health professionals and patients, and these should be taken into consideration when adapting international recommendations to the national setting. The establishment of an effective collaboration between health services and society often requires building the capacity of communities and civil society organizations, fostering a continuous dialogue and involving them from the start in designing, planning, implementing and evaluating community initiatives.

Effective community and patient involvement yields positive results, such as improved case-finding and treatment outcomes, raised awareness concerning the nature of the disease and the availability of effective treatment free of charge, or general health promotion. To be successful, community and patient involvement initiatives should be designed and implemented with community members involved as equal partners.

26.1 Key steps in implementing initiatives for community and patient involvement

26.1.1 Policy guidance

The development of guidance for policy involves:

- setting up a task force to conduct a situation analysis and draft policy guidance;
- testing policy guidance in demonstration areas.

In countries with no existing initiatives to involve communities, i.e. where the initiative to set up such activities comes from the central level, it is important to have policy guidance based on a national situation analysis. This approach promotes community ownership of the initiative, and encourages the community's active involvement and shared responsibility for health.

The policy guidance should describe a process of involvement of local communities and tuberculosis patients, and should introduce the use of indicators of community involvement, such as participation in planning, support and evaluation of the intervention, role in improvement of case detection and treatment adherence, impact on stigma and discrimination, promotion of healthy lifestyles and quality of care as perceived by patients and their families.

26.1.2 Advocacy and communication

Activities for advocacy and communication involve:

- advocating at central level and locally with different stakeholders (health managers, politicians, community leaders, etc.) for TB control and community involvement;
- designing communication tools tailored to the local context.

Presenting the initiative to relevant officials at the central and local levels is an important step in setting up community-based activities. This encourages involvement of all stakeholders as well as political and financial support. Communication tools for promoting messages on TB will depend on the target population and the availability of resources. To ensure that the content of the communication material is tailored to the local context, it should be developed with the community and pretested in the target population (see also Chapter 27).

26.1.3 Capacity building

Building the capacity of human resources involves:

- quantifying the shortage in human resources and identifying solutions;
- developing training material for health staff and local communities and conducting regular training;
- creating partnerships with ongoing community-based initiatives (NGOs, faith-based organizations, community-based organizations).

Capacity building and training of people involved in the initiative, within and outside the health sector, are essential. Training should take into consideration the roles and

responsibilities of different stakeholders. It is important to discuss with the community their future role, with the aim of strengthening both the community and the health system. Cured TB patients are often willing and motivated to be involved in TB control activities such as treatment support and combating TB-related stigma. Setting up partnerships with ongoing community-based initiatives in the area (NGOs, faith- and community-based organizations) has proved, in most countries, to be more sustainable and cost-effective than creating parallel systems.

26.1.4 Addressing special challenges

The challenges of TB/HIV, MDR-TB, and special groups and situations involve:

- exploring opportunities for the roles of patients and local communities in addressing special challenges.

At national and local levels, experience has shown that community involvement can make a valuable contribution to addressing special challenges such as TB/HIV, MDR-TB, controlling TB among indigenous populations or ethnic minorities, in congregate settings, etc. (see Chapter 25).

26.1.5 Ensuring high-quality services at community level

Ensuring the high quality of services at the community level involves:

- identifying the range of services available at community level;

- ensuring an adequate referral system; identifying people (e.g. public health workers, community representatives or volunteers) who will provide a link between health services and local communities/patients;
- providing regular support to community-based activities.

A routine supervision system to monitor and support the services and care provided at community level should be established. Motivation of the involved community members is encouraged by regular support.

The range of services provided at community level should be tailored to community and patient needs, rather than to the convenience of the health services. In settings where there is no existing community involvement initiative, it is important to identify people who are able to provide an effective link between health services and local communities.

26.1.6 Budget and financing

Measures for budget and financing involve:

- identifying a comprehensive list of expenditures at all levels related to community involvement;
- ensuring that sufficient funds are available for community involvement (e.g. ensure that such costs are included in local health budgets).

Resources for community-based activities should come from different sources, and not exclusively from the ministry of health budget. External (such as the Global Fund) and

internal sources of funding (local partners providing ongoing support) should also be explored. In settings where the community is involved in a range of health issues and services, duplication of budget lines and activities should be avoided.

26.1.7 Monitoring, evaluation and supervision plan

The development of a monitoring, evaluation and supervision plan involves:

- defining a set of indicators, separating those to be collected on an ongoing basis and those to be collected every one or two years.

Communities should participate in the assessment of their own contribution and that of the health services. The data collected should be limited to the essential information that will be analysed and used for assessing services and community involvement. Indicators to monitor community involvement should reflect organization, representation, perceived quality of services and sustainability. Patient satisfaction, TB-related knowledge and TB-related stigma may be assessed through a KAP (knowledge, attitudes and practices) survey every one or two years.

26.1.8 Operational research

Planning for operational research involves:

- identifying operational research themes based on local challenges and opportunities (e.g. conducting research on patient satisfaction, documenting good practices).

Operational research may be required to address specific operational issues and improve community involvement. Both qualitative and quantitative research methods should be considered when assessing the outcome of activities as well as perceptions and motivation at the community level.

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Chapter 27 Advocacy, communication and social mobilization

Component 5 of the Stop TB Strategy urges enhancement of ACSM at country level to improve case detection and treatment adherence, to combat stigma and discrimination, to empower people affected by TB, to mobilize political commitment and resources for TB control, and to institute social change and poverty reduction required for long-term control and elimination of TB. Many of the global ACSM approaches have focused, quite successfully, on mobilizing resources and strengthening political and governmental commitment. However, there is an urgent need to intensify communication efforts and to foster the broader engagement of civil society in control and elimination of TB (Box 27.1).

BOX 27.1

FIVE-POINT FRAMEWORK FOR ACTION ON ADVOCACY, COMMUNICATION AND SOCIAL MOBILIZATION (ACSM) AT COUNTRY LEVEL

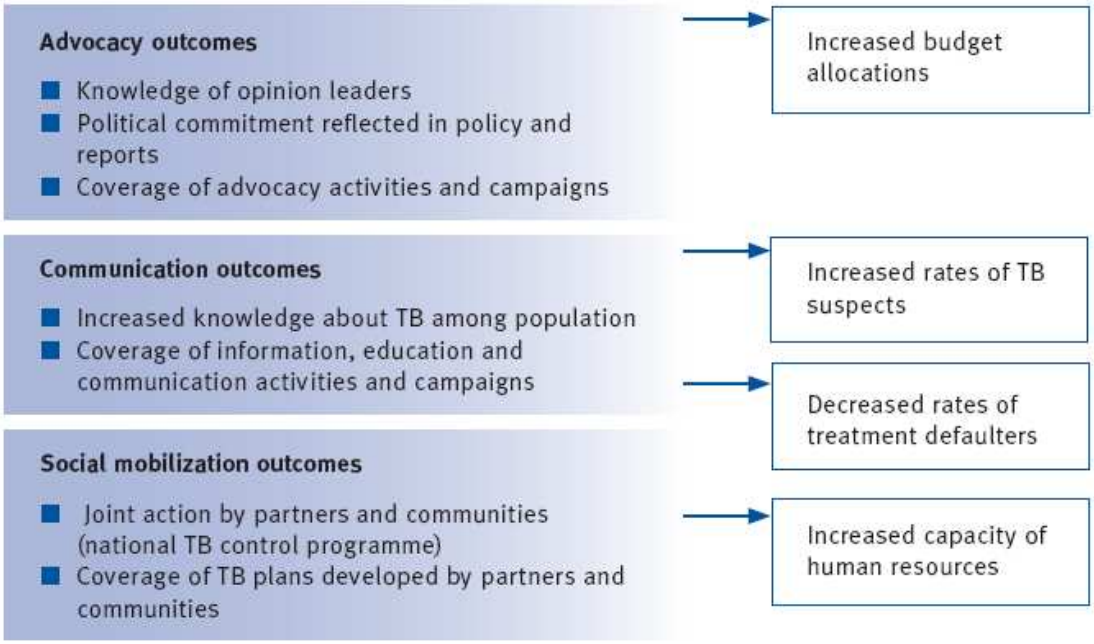
1. Building national and sub-national ACSM capacity
2. Fostering inclusion of patients and affected communities
3. Ensuring political commitment and accountability
4. Forging country-level ACSM partnerships within the context of national tuberculosis control programmes
5. Learning, adapting and building on good ACSM practices and knowledge exchange

ACSM involves three distinct sets of activities, all of which have the shared goal of bringing about behavioural change. One of the major distinctions between them is the target audience.

Advocacy works primarily to change the behaviour of public leaders or decision-makers. *Communication* generally targets individuals and small groups. *Social mobilization* aims to secure community-based support.

The distinction between the three categories is often unclear, and interventions under one area may beneficially influence or facilitate processes in the other areas. ACSM is an important ally in TB control efforts and should be an integral, funded element in any TB control programme (Figure 27.1).

FIGURE 27.1 SAMPLE MONITORING AND EVALUATION FRAMEWORK FOR ADVOCACY, COMMUNICATION AND SOCIAL MOBILIZATION



27.1 Advocacy and resource mobilization

Political commitment has been recognized as a crucial element of the DOTS strategy. Lack of political will has hampered both the development of appropriate TB control policies and the successful implementation of those policies at the central, district and local levels.

In the global context, advocacy for TB control is to be understood as a broad set of coordinated interventions directed at placing TB control high on the political and development agenda, to secure international and national commitment and mobilize necessary resources. At the country level, advocacy broadly seeks to ensure that national governments remain strongly committed to implementing national TB control or elimination policies.

Advocacy at country level often focuses on administrative and corporate mobilization through parliamentary debates and other political events; press conferences; news coverage; TV and radio talk shows; popular TV series; summits, conferences and symposia; celebrity spokespeople; meetings between various categories of government and civil society organizations, patients organizations and health-care providers; official memoranda; and partnership meetings.

27.2 Communication

Within countries, and in the context of TB control, programme communication is concerned with informing and creating awareness among the general public or specific population groups about TB, and empowering people to take action. It is often mainly concerned with communicating a series of messages about the disease (e.g. “if you have a cough for more than two weeks, seek treatment”, or “TB is curable”), or informing the public about which services exist for diagnosis and treatment.

27.3 Social mobilization

Social mobilization is the process of bringing together allies to raise awareness of and demand for a particular programme, to assist in the delivery of resources and services and to strengthen community participation for sustainability and self-reliance (see also Chapter 26). "Allies" include decision- and policy-makers, opinion leaders, NGOs such as professional and religious groups, the media, the private sector, communities and individuals. Social mobilization generates dialogue, negotiation and consensus, engaging a range of players in interrelated and complementary efforts, taking into account the needs of people (Box 27.2).

BOX 27.2

KEY STEPS FOR IMPLEMENTATION OF ADVOCACY, COMMUNICATION AND SOCIAL MOBILIZATION (ACSM) ACTIVITIES AT NATIONAL, DISTRICT AND PROVINCIAL LEVELS

1. Create a national partnership or task force
   - ✔ Charged with planning, implementing and evaluating all activities
2. Conduct an ACSM needs assessment
   - ✔ Review epidemiological data
   - ✔ Identify priority populations
   - ✔ Identify key social determinants of TB
   - ✔ Determine behavioural goals
   - ✔ Determine social change goals
3. Develop a workplan and budget
   - ✔ Match goals and targeted audiences with activities
   - ✔ Establish benchmarks and process or impact indicators
4. Implement activities
   - ✔ Develop, pre-test and produce materials
   - ✔ Organize advocacy events, social mobilization activities, etc.
5. Monitor and evaluate results
   - ✔ National/district/provincial levels

27.4 Monitoring and evaluation

Increasingly, ACSM strategies contain a monitoring and evaluation mechanism that is critical to building a stronger evidence base for measuring process, output and impact of

ACSM strategies for TB control. NTP staff are encouraged to develop a qualitative and quantitative monitoring and evaluation strategy for ACSM activities.

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Chapter 28 Role of national tuberculosis control programmes in research

Research across a wide spectrum of areas is necessary to accelerate progress in global TB control and enable the revolution in technologies for TB control needed to achieve the goal of eliminating the disease by 2050. Key areas of research include:

- *applied research,* i.e. optimizing the use of current approaches to TB control through epidemiological, programmatic, health systems, health economics, and social and policy research;
- *development of new tools,* i.e. research and development (R&D) for new diagnostics, drugs and vaccines;
- *evaluation and demonstration of new tools* (diagnostics, drugs and vaccines);
- *basic research,* i.e. improving understanding of the basic science that underpins the development of new tools.

28.1 National TB control programmes and the Research Movement to Stop TB

Recognition of the importance of TB research is reflected in the Stop TB Strategy. The Research Movement to Stop TB, mandated in 2006 by the Stop TB Partnership and WHO, represents an opportunity to engage the full range of TB researchers in a collaborative strategic effort to increase the scope, scale and speed of TB research. The success of the Research Movement as a broad alliance of all those involved in TB research depends on engaging the full range of researchers in basic research, R&D and applied research (including the NTPs).

28.2 Applied research

Making the most of current approaches to TB control depends on the contribution of many areas of applied research: epidemiological, programmatic (operational), health systems, health economics, and social and policy research. Research in these areas should involve NTPs, since the aim is to improve programme performance. NTPs have a crucial role to play in designing and carrying out operational research that involves the evaluation of programme operations aimed at improved policy-making, better design and operation of health systems and more efficient methods of service delivery. The NTP should develop effective collaboration with researchers from academic or other research institutions who often play the lead role in carrying out operational research.

28.3 Development of new tools for TB control

Progress in global TB control is constrained by the lack of effective new tools (diagnostics, drugs and vaccines). The Stop TB Partnership and WHO are promoting the development of better technologies for preventing, and improving the diagnosis and treatment of, TB through the Partnership's three working groups on new tools development. These working groups (on new diagnostics, drugs and vaccines) aim to provide better technologies for preventing TB, and to accelerate the process of diagnosis and treatment, especially in regions where TB/HIV and MDR-TB make TB control particularly difficult. The Stop TB Strategy emphasizes the need to develop better technologies for preventing, and improving the diagnosis and treatment of, TB at affordable cost for developing countries. Creative intellectual property mechanisms are

being developed that protect the public health sector and enhance access to new technologies by underprivileged patients.

In 2006, the Stop TB Partnership Coordinating Board established a Task Force on Retooling to respond specifically to the need to prepare for the launch of new TB technologies.[1] "Retooling" is the process of introduction, adoption and implementation of new and improved diagnostics, medicines and vaccines, with the goal of maximizing their widespread use while minimizing delays. To be successful, the retooling process involves the participation of a wide range of stakeholders at the global and country levels and the consideration of a number of key components, including an assessment of a country's capacity to adopt and implement a new technology.

28.4 Evaluation and demonstration of new tools

NTP managers need to keep abreast of research developments. The NTP has an essential role in the establishment of clinical trial platforms for the evaluation and demonstration of new tools (diagnostics, drugs and vaccines). Clinical trials require standard ethical approval. As new tools become available, NTP managers will be involved in the process of ensuring their smooth and rapid transition directly to the field. Preparations for incorporating new tools into NTP activities include regulatory approval of new tools, developing purchasing mechanisms and training the health-care workers who will use and administer them in the field.

[1] See www.stoptb.org/retooling

28.5 Basic research

More basic research is necessary to address fundamental gaps in the science and understanding of the biology and pathogenesis of *M. tuberculosis*. Advances in basic TB research are needed to generate the discovery of new agents to sustain the pipeline of research and the development of new tools. Through the Stop TB Partnership, NTPs may play a role in advocating for increased investment in fundamental scientific research on TB to fortify the foundations of knowledge that will lead to key advancements in the field.

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Annex Strategy for the control and elimination of tuberculosis

Introduction

The Stop TB Strategy (2006–2015) paves the way for controlling tuberculosis (TB) and, beyond, towards the long-term goal of eliminating the disease as a global health problem by 2050. TB elimination is defined as achieving an incidence of less than 1 case of infectious TB per million population or a prevalence of latent TB infection of less than 1%. Several countries have already reached the TB elimination phase; others are expected to do so in the foreseeable future. The TB elimination phase is defined as an incidence of fewer than 20 cases per 100 000 population.

The strategy for TB elimination involves the implementation of interventions additional to standard TB control measures. It is not only relevant to countries with a low incidence of the disease that are approaching the elimination phase but should also be considered by countries with an intermediate and steadily decreasing TB incidence (i.e. <50 cases per 100 000 population).

This annex provides an overview of the essential prerequisites for TB elimination, describes some relevant interventions for countries in the elimination phase and examines the challenges involved in planning for TB elimination. Country examples from Cuba (Box A1), Italy (Box A2), the Netherlands (Box A3), Slovakia (Box A4) and the United Kingdom (Box A5) illustrate the relationship between epidemiological trends and implementation of interventions for TB elimination.

As a result of globalization, the elimination of TB in low-incidence countries will depend upon the achievement of global TB control. It is therefore essential that these countries continue to support the implementation of effective TB control in high-incidence areas and settings, in parallel with the introduction of elimination strategies.

A1.1 Strategy for control and elimination

The Stop TB Strategy sets out the key steps for comprehensive TB control. The focus for the elimination of TB in low-incidence countries and the priorities for implementation of the TB elimination strategy involve some modification of the standard approaches to TB control. During the elimination phase emphasis needs to be placed on interventions for (i) high-risk group management, (ii) outbreak management and (iii) infection control.

A1.1.1 Management of high-risk groups

The management of high-risk groups involves the identification of specific population groups who are at increased risk of TB (or TB infection) and the implementation of strategies for active TB case-finding as well as the identification of latent TB infection, ensuring provision of supervised and supported treatment, and monitoring of treatment outcomes. The policy for high-risk group management should specify how risk groups are defined in the country or region, e.g. by epidemiological characteristics such as a specified threshold of TB incidence or high prevalence of risk factors for TB (recent immigration from high TB incidence countries, deprivation, alcohol and substance misuse, malnutrition, homelessness) and/or by cost-effectiveness considerations.

A1.1.2 Screening for active TB

Screening for active TB should be offered regularly to individuals in high-risk groups, and all cases should be adequately treated, including treatment support and monitoring of treatment outcomes. Many individuals in high TB risk groups are also at increased risk of treatment default owing to other characteristics such as chaotic lifestyles, psychological disturbances, homelessness, immigration/legal status and high mobility. These individuals require intensive treatment support and supervision (including directly observed therapy, or DOT). Enough staff and resources (including time, transport facilities and enablers) should be available to meet the needs of these particular high-risk groups. Monitoring the outcome of treatment is essential for evaluation of the yield of screening and the overall result of the intervention. The proposed targets for high-risk groups are to screen 95% of the population and to obtain 95% treatment success. In addition, all close contacts of infectious TB cases should be screened.

Screening of some high-risk groups such as illegal immigrants may involve additional problems because these individuals are not easily reached by the health system. Access to services should be facilitated and incentive schemes provided in order to reduce diagnostic and treatment delay as much as possible.

A1.1.3 Screening for TB infection

Screening for latent TB infection using tuberculin skin testing and/or interferon gamma release assays should be carried out regularly in high-risk groups, and positive individuals should be offered preventive therapy, including treatment support and monitoring of treatment outcomes.

Some groups that should be prioritized for latent TB screening are:

- *Contacts of patients with infectious TB*. Effective contact tracing to identify and screen all individuals directly exposed to an active TB case as well as regular screening of other individuals at increased risk because of their frequent contact with high-risk groups.

- *Professional contacts of high-risk groups*. Occupational health departments should offer regular screening to all staff who have frequent professional contact with members of any high-risk group, particularly if case-finding in the risk group reveals a high incidence of smear-positive TB.

- *Individuals with risk factors/co-morbidity for developing active disease*. Individuals at risk of developing active TB should receive special preventive care. Epidemiological analysis of sensitivity, specificity and positive and negative predictive values might help determine lower cut-off values for the diagnosis of latent TB infection in these groups.

A1.1.4 Management of outbreaks

Adequate surveillance systems should be in place to ensure early identification of outbreaks. Epidemiological analysis of TB cases and DNA fingerprinting, which enables the confirmation of clusters of patients with the same bacterial strain, may help identify links between patients, suggesting groups or situations where transmission might have occurred. Additional interventions such as infection control measures may then be taken to prevent further transmission.

A1.1.5 Measures to control infection

Infection control measures are necessary to prevent the transmission of *M. tuberculosis* in congregate settings such as hospitals, prisons and shelters for homeless people. Effective infection control measures vary from simple adequate ventilation and isolation facilities to ultraviolet light and negative pressure rooms (see Chapter 6). Implementation of these measures should be guided by evidence of effectiveness, degree of severity of the disease (e.g. multidrug-resistant TB or extensively drug-resistant TB), risk or susceptibility of the population (e.g. human immunodeficiency virus status) and data from cost-effectiveness studies. Identifying factors that may contribute to transmission from potentially infectious cases and instituting adequate control measures are of primary importance.

A2.1 Prerequisites for the elimination strategy

Essential prerequisites for countries entering the elimination phase have been proposed in the *European framework for TB control and elimination in countries with a low incidence*. Countries planning to start implementing the TB elimination activities should

have reached a TB incidence of fewer than 20 cases per 100 000 population, with a downward trend. The requirements for TB elimination are outlined below.

A2.1.1 Government commitment

Government commitment and continued support of national structures for TB control and elimination are essential, particularly because there is a danger that once the country reaches a low incidence status other priorities will prevail over the maintenance of TB control. Engaging and involving politicians and public health policy-makers in TB elimination is a major task during the elimination phase.

A2.1.2 National structures for TB elimination

Most low-incidence countries do not have a formal national TB control programme. However, other alternative structures are often present.

- An authoritative central body that reviews and develops evidence-based guidance for TB control and elimination. This is not necessarily a governmental institution and, in many countries, it could be an independent group of academics or professionals that develops and endorses policies and guidelines covering case-finding, standardized treatment, implementation of high-risk group management, and infection control policies. This *national TB control policy committee* should include scientific, practical and administrative expertise.
- The compilation of policies and guidelines constitutes the *national policy for TB control and elimination*.

- A *national support unit*, often formed by a team of experienced experts at central level, should oversee the implementation of national policy, coordinate adequate surveillance, provide support and supervision, and evaluate the performance of national control activities.

- The *national TB control network* of professionals involved in daily TB control activities should be recognized as such and financially supported. The triangle of front-line (hospital) clinicians, bacteriological laboratories and regional (TB) public health specialists is vital to this control network. The TB control network should also include key individuals at the ministries of health and justice, social services, national reference laboratory and other relevant institutions.

- Evaluation of results of the regional TB control measures and policy should be done regularly by an external independent team of experts. Likewise, at least once every five years, a countrywide audit or review should be done by an independent team of national and international experts.

A2.1.3 Legal framework

The existence of an appropriate legal framework is essential for control and elimination of TB. The legal framework should include notification of cases; reporting of *Mycobacterium tuberculosis* isolates and sensitivity patterns, including the performance of DNA fingerprinting (including without consent of the patient under specified

conditions); financing of active and passive case-finding; financing of TB treatment, including financial support and accommodation to illegal immigrants during treatment; infection control; legal powers and procedures for compulsory isolation for diagnosis and treatment in non-compliant individuals.

A2.1.4 Surveillance and monitoring

Maintenance of an extensive surveillance and monitoring system according to international recognized standards, tailored to the national or regional situation, is the backbone of the TB elimination strategy. It should provide prompt information on the diagnosis and treatment outcome of all cases, as well as the results and yield of contact tracing and high-risk group management activities.

A2.1.5 DNA fingerprinting

Routine nationwide DNA fingerprinting provides important information during the elimination phase: (i) it helps the identification of epidemiological links between patients and suggests patterns of transmission, sometimes undetected through traditional contact investigations; (ii) it shows where transmission continues to occur in regions or countries with low numbers of cases; (iii) it supports the identification of specific high-risk groups in clusters where infection continues to spread despite traditional control measures and for which other interventions should be considered; and (iv) it helps to identify laboratory cross-contamination, giving important information on the quality of laboratory performance, particularly in those that may handle only small numbers of specimens in regions with few suspect or TB cases.

A2.1.6 Accessible services

Access to diagnostic and treatment services should be made easy, particularly for those individuals in high-risk groups: immigrants (legal and illegal), the homeless and individuals dependent on alcohol and illegal substances. Services should also be culturally sensitive, and the lack of health insurance or identification documents should not be an impediment to access to the health system. Once TB is diagnosed, special arrangements for risk groups with specific difficulties should be made to facilitate treatment success.

A2.1.7 Trained staff

Adequately trained staff with the essential knowledge, skills and attitudes should be available at all levels. An educational plan for the different professionals involved in TB elimination should be available, including clinical, microbiological and public health skills as well as staff in social services. Training in intercultural communication is essential, since rapid case-finding and successful treatment are largely dependent on it.

A2.1.8 Health information

Culturally-adapted health information materials should be available. This information is directed towards reducing delays in diagnosis, promoting high participation in screening programmes and supporting treatment success. Transmission of the information to specific groups should be carried out in a manner appropriate to the groups concerned.

A2.1.9 International cooperation

International cooperation is important, particularly in small or medium-sized countries with a low incidence of TB (<5 cases per 100 000 population) where the number of TB cases is very small. Adoption of regional policies and international intercountry cooperation and support with exchange of experiences and information, including the use of international experts in the process of agreeing regional policies and shared surveillance systems, may also contribute to solving common problems and ensuring adequate elimination.

A1.3 Challenges

Progressive adaptation of the organization of TB control to a lower case-load while maintaining expertise and commitment presents major challenges in countries with a low and declining TB incidence. Specific issues requiring consideration are outlined below.

A1.3.1 Projecting trends

Adaptation of the structure and organization of TB control to a substantially lower case-load requires projection of trends over a 20–30-year period. In many low-incidence countries, immigration is the most important factor slowing down (or even reversing) the decline of TB incidence in the general population. Different levels of immigration should therefore be included in modelling future trends. Diverging TB incidences between cosmopolitan cities and more remote regions of the country should also be considered.

A1.3.2 Special measures

Measures such as the reorganization of TB control services may be needed when a decline in TB cases is likely to occur. Centralization of expertise is a logical approach when numbers of cases are decreasing, but good access to diagnosis and treatment services at the peripheral level will continue to be needed. Countries in the elimination phase will have to deal with the centralization of expertise while maintaining good, decentralized access.

A1.3.3 Case-finding

While active case-finding is pivotal within high-risk groups, passive case-finding of symptomatic cases will remain the most important way to identify new TB cases in the community. Strategies to maintain standards for diagnostic services and to prevent diagnostic delays will be needed. Laboratory services should be supervised by expert professionals to fulfil requirements of quality and safety. A process of centralizing laboratory activities in a few laboratories in the country may be envisaged, based on consultations involving national expert centres and the mycobacterial reference laboratory.

Organization of active case-finding should be considered for countries that are approaching 1 case per 100 000 population. Screening for TB and for latent infection should be continued in high-risk groups, including in contacts of TB patients.

A1.3.4 Maintaining expertise

Both treatment and treatment supervision require skills that are difficult to maintain when very few cases occur each year. Maintaining the TB expertise of chest physicians, microbiologists and public health doctors and nurses is a challenge for all professional groups. Two levels of expertise may be envisaged: a lower level for those who may occasionally encounter a TB case (pulmonologists, other clinicians and general public health specialists), and a higher level for some diagnostic and treatment specialists and leaders of regional and national TB control programmes. These experts may be trained together and, where appropriate, in collaboration with other countries. Responsibility for the treatment and supervision (including DOT) in regions with a low TB incidence (e.g. <2 cases per 100 000 population) should be clearly defined.

A1.3.5 New interventions

New interventions should be considered for countries to accelerate the decline in the number of TB cases. An effective vaccine would be the most important tool for TB elimination, but this is unlikely to be available in the short term. Reducing the prevalence of latent TB infection through active screening and preventive therapy should be considered.

Box A1 Application of the strategy to eliminate tuberculosis in Cuba

In pursuing its strategy for TB elimination, Cuba focuses on the following 10 measures:

1. Maintaining government commitment to sustain the priority of the national TB control programme (NTP) among other health programmes in order to ensure continued support for national structures for TB control and elimination.

2. Developing a wide network of health centres based on family physicians who provide care and preventive measures free of charge nationwide (120 families per physician), thereby strengthening DOT and TB control.

3. Social security that allows people living with TB to receive 100% payment without working during the whole period of treatment and a supplementary diet at subsidized prices.

4. Educational plan for the different involved professionals with the essential knowledge, skills and attitude, to assure trained staff and development of expertise in both treatment and treatment control, in order to improve treatment success even in regions with low TB incidence.

5. Active participation of the involved community and people living with TB.

6. Strengthening collaboration between the programme to control sexually-transmitted infections and HIV and the NTP in primary health care settings, as well as in the secondary and tertiary health care system, as part of a comprehensive approach to pulmonary health care.

7. Monitoring and evaluation of treatment outcomes and anti-TB drug resistance; provision of routine nationwide DNA fingerprinting to identify patterns of transmission and assess quality of performance of laboratories.

8. Preventive treatment for every TB contact and for people living with HIV/AIDS.

9. Offering an HIV test free of charge to every person living with TB.

10. Improving health education for communities with higher incidence or prevalence rates and high-risk groups such as prisoners.

Box A2 Strategy for eliminating tuberculosis in Italy

Italy notified only 7 new TB cases (3 sputum smear positive) per 100 0000 population and a prevalence of latent infection below 1% in young cohorts (aged <18 years) in 2005 and is approaching the elimination phase. Guidelines and a legal framework were developed in the early 1990s aimed at improving risk-group management, outbreak management and infection control in congregate settings. Since 1990, all TB cases must be notified by both clinicians and laboratories. The National TB Study Group of the *Associazione Italiana Pneumologi Ospedalieri* (AIPO) promoted development of comprehensive guidelines on TB control, discussion within the scientific and public health community and evaluation of their impact.

Government commitment is attested by the legal adoption of these guidelines and the establishment of centres for disease control, acting as a framework for a National TB Commission nominated by the Ministry of Health (including representatives of scientific societies, TB control, microbiologists and other experts). The main task of the Commission is to revise policies and guidelines for TB control and elimination, and to coordinate the surveillance, laboratory and clinical network. In 2004, the strategic plan was approved; it includes the following eight key actions:

1. Improving knowledge of TB among health staff and civil society (to reduce both patient and physician delays).

2. Strengthening surveillance and monitoring and increasing coverage to all 21 regions of the country.

3. Establishing a special register of MDR-TB cases.

4. Using monitoring and evaluation indicators targeting special challenges (e.g. treatment success of at least 85% of cases aged <65 years and reducing the proportion of treatment defaulters to less than 8%).

5. Improving quality control of the laboratory network (including DNA fingerprinting of all drug-resistant cases).

6. Defining standards of care.

7. Increasing access to, and cultural sensitivity of, health services.

8. Developing adequate human resources (through increased collaboration with the international cooperation department of the Ministry of Foreign Affairs).

The coordination of different governmental and nongovernmental stakeholders was further enhanced by the establishment of Stop TB Italia in 2004.

The main challenge to be faced in the near future is to increase coordination among different stakeholders and with the 21 regional governments.

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Box A3 Towards elimination of tuberculosis in the Netherlands

The Netherlands attained low TB prevalence in 1971, with an annual incidence of fewer than 20 cases per 100 000 population, partly as a result of mass X-ray screening in the 1950s and 1960s. In the 1980s and 1990s, the strategy comprised prompt diagnosis and treatment of symptomatic cases, contact tracing around infectious TB cases and screening of immigrants. In the 1990s, a more explicit policy for management of risk groups was formulated, and nationwide DNA fingerprinting of all strains was introduced. In 2006, 75% of TB cases were detected by passive case-finding and 25% by screening risk groups.

1. Risk group management

Screening for active TB
- Newly arrived immigrants and asylum seekers: obligatory at entry and periodically for people from countries with a TB incidence >200 cases per 100 000 population;
- injecting drug users: once or twice a year, depending on local circumstances;
- homeless people: once or twice a year, depending on local circumstances;
- prisoners: once on incarceration;
- contacts of infectious patients: once or periodically;
- professional contacts of risk groups: periodically.

Risk group management includes intensive supervision (DOT) by TB nurses of the municipal health services for all patients with potentially low compliance (asylum seekers, injecting drug users, the homeless, illegal immigrants, children, relapse cases, resistant cases) and treatment outcome monitoring for each risk group.

Screening for TB infection and preventive treatment
- Contacts of infectious TB patients
- Professional contacts of risk groups (periodically)
- Persons with a risk factor (co-morbidity) for breakdown to active disease
- Travellers to endemic areas.

2. Outbreak management
- Countrywide DNA-fingerprinting of all culture-positive isolates.
- Follow-up of epidemiological links to identify growing clusters and unobserved transmission.

3. Infection control
- Adequate isolation of infectious patients in both inpatient and outpatient settings.
- Adequate institutional infection control measures

Prerequisites for effective TB control and elimination are in place supporting national and decentralized structures:

- *National TB control policy committee*. Quarterly meeting of independent group of professionals with scientific, practical and administrative expertise in TB control.
- Compilation of national TB policy for control and elimination.
- *National support unit*. Experts at central level to coordinate and facilitate implementation, execute surveillance, provide support and supervision, and evaluate the performance of national control activities.
- Evaluation of results of the regional TB control policy: national and international review of TB control every five years.
- *Surveillance and monitoring*. Comprising (i) web-based collection of individual diagnostic data, treatment outcomes and results of contact investigation for all TB patients and (ii) monitoring system for screening programmes.
- Free accessible TB services at municipal health service and hospitals.
- Operational research to develop and evaluate TB control interventions.

Box A4 Strategies for control and elimination of tuberculosis in Slovakia

A systematic approach to the treatment of TB started in Czechoslovakia in the middle of the 20th century. The National TB Management Committee – an advisory body established by the Ministry of Health – is now responsible for providing guidance on control and elimination of TB in Slovakia. The Ministry endorsed a legal framework for TB control that allows health-care professionals to enforce isolation, diagnosis and treatment of non-compliant patients. The national coordination centre for TB is located in the National Institute for Tuberculosis, Lung Diseases and Thoracic Surgery. A national TB register with individualized data on TB patients has been in use since 1988; an MDR-TB unit was created in 1998. There is a link between reports provided by clinicians and the laboratories on case-finding of smear- and culture-positive TB. The national guidelines are regularly updated to address new developments in TB control and incorporate new WHO recommendations.

1994 – Implementation of the DOTS strategy
1998 – Implementation of the new reporting system
2006 – Introduction of new diagnostic methods for screening for TB infection

Contact investigation is carried out for contacts of infectious TB patients, professional contacts of risk groups and people with risk factors for TB. Latent TB infection is detected by tuberculin skin testing and interferon gamma assays. Individuals with positive screening results receive preventive therapy. All patients with confirmed TB are admitted for the initial phase of treatment to facilitate DOT. Each general practitioner is familiar with the system of TB management and knows where to refer patients with suspected TB.

Treatment of drug-resistant TB is managed by pulmonary specialists, and DOT is provided throughout treatment. If surgery is required, it is undertaken in one of the two specialized hospitals.

The group at greatest risk of TB in Slovakia is the Roma population (approximately 8% of the total population). A special approach to ensure continuity of TB treatment is applied through the use of TB Roma assistants operating in the Roma settlements to facilitate DOT and ensure treatment completion.

Implementation of this systematic approach has led to the gradual reduction of TB incidence, which reached 13.2 per 100 000 population in 2006.

Challenges. With the decreasing number of patients requiring TB medication, there is a growing concern that pharmaceutical companies will lose interest in marketing essential anti-TB drugs. The shortages of these essential medicines would have dramatic consequences on the process of TB elimination in Slovakia.

Box A5 Focusing on high-risk groups for the elimination of tuberculosis in the United Kingdom

Control of TB in the United Kingdom is patient-centred and takes account of the patient's individual needs and preferences. It is based on evidence-based guidelines commissioned by the National Institute for Health and Clinical Excellence.

Treatment adherence. All patients are assessed for risk factors for treatment default to identify those requiring additional support. Patients are involved in all treatment decisions. Each patient has a designated health worker and receives information leaflets (available in all relevant languages). Street- or shelter-dwelling homeless people receive incentives for treatment adherence, such as temporary accommodation.

MDR-TB risk assessment. All cases are assessed for drug resistance using sputum culture on liquid media and tested for first-line drug sensitivity. Treatment response is closely monitored in suspected cases. MDR-TB care is coordinated by specialists taking into account the views of patients and including shared care.

High-risk group screening

1. New arrivals are identified for TB screening (i) when entering the country (port-of-arrival report), (ii) when registering with primary care, (iii) at entry to education (including universities) and (iv) through links with voluntary and statutory organizations working with illegal immigrants, refugees and asylum seekers. Screening is usually carried out once.
2. The street homeless, including those using direct-access hostels, are opportunistically screened or when symptomatic, and simple incentives such as hot drinks and snacks are used. Social workers and other staff working with these groups are aware of TB and its symptoms.
3. Staff working with high-risk groups have a complete TB screen. All new National Health Service staff have an assessment of personal and family history; a symptoms and signs enquiry; documentary evidence of TB testing and/or BCG scar checked by occupational health and/or tuberculin skin test result within the past five years if available.
4. Prison and remand centre staff are trained in knowledge of TB symptoms, and promote awareness among prisoners and other staff. Prisoners are screened on entry using a health questionnaire and, if positive for signs and symptoms, receive a chest X-ray and sputum smear examination.

BCG vaccination. Neonatal vaccination is offered soon after birth for all babies at increased risk, after discussion with parents or legal guardians.

Contact tracing. Contact tracing is done in all cases of active TB; contacts are screened for active and latent TB.

Challenges. Many patients acquired TB outside the United Kingdom and present a combination of risk factors for treatment default such as homelessness, alcohol and substance dependency, illegal status and high social needs. These patients require intensive resources and a multidisciplinary team providing a complete network of services to ensure successful treatment.

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