TUBERCULOSIS

WORLD HEALTH ORGANIZATION
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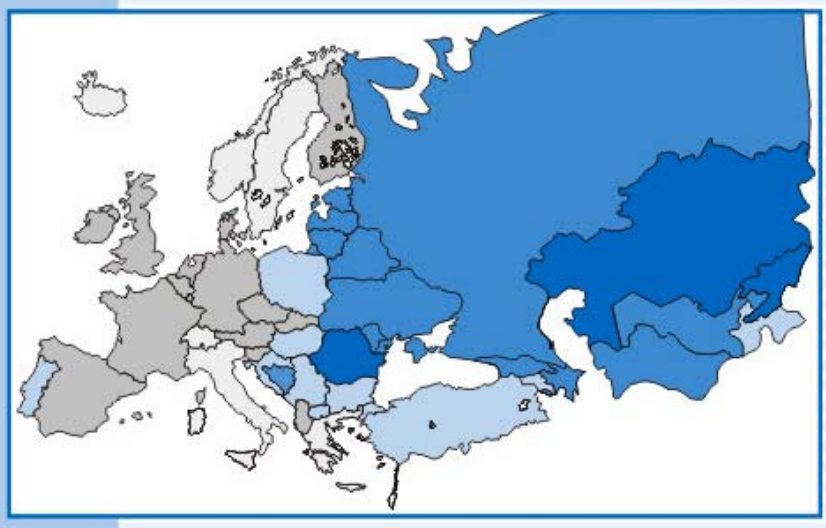

Brief Guide on Tuberculosis Control for Primary Health Care Providers

For Countries in the WHO European Region with a High and Intermediate Burden of Tuberculosis

New Jersey Medical School
National Tuberculosis Center
A Founding Component of the International Center for Public Health

BRIEF GUIDE ON TUBERCULOSIS CONTROL FOR PRIMARY HEALTH CARE PROVIDERS

FOR COUNTRIES IN THE WHO EUROPEAN REGION WITH A HIGH AND INTERMEDIATE BURDEN OF TUBERCULOSIS

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ABSTRACT

Tuberculosis is an increasingly serious problem in the WHO European region, particularly in the countries of eastern Europe, the Baltic States, and the Commonwealth of Independent States (CIS). Primary health care providers can play an important role in tuberculosis control through early detection of the disease, referral for treatment, and involvement in directly observed treatment. This guide has been written with the aim of developing the knowledge, awareness and skills of primary health care providers regarding tuberculosis and its prevention and control. The guide is not intended as a complete source of information on tuberculosis, but rather a summary of general principles regarding prevention, detection and treatment. The guide does not reflect specific national guidelines on TB control, and is intended to be used in conjunction with the appropriate national regulations. A reference card containing key information is included with this guide.

Keywords

TUBERCULOSIS- prevention and control
TUBERCULOSIS, MULTI-DRUG RESISTANT – prevention and control
GUIDELINES
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[1] United States Agency for International Development
[2] Centers for Disease Control and Prevention
[3] New Jersey Medical School National Tuberculosis Center
[4] Public Health Research Institute
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How to Use This Guide

This guide is intended for primary health care (PHC) providers in the WHO European Region who deliver care at the first point of patient entry into the health care services. This may include medical workers at health units in factories or other work environments in addition to workers at hospitals, polyclinics and feldsher and midwife posts (FMPs). It encompasses the work of PHC physicians including therapeutists, general practitioners and family practitioners, as well as private physicians and feldshers.

Though physicians and feldshers are the primary audience of this guide, nurses may also find the information useful. Because this is a very broad audience geographically and professionally, it would be very difficult to create one comprehensive source of information that provides specific details and guidance for all readers. Thus, this guide is not intended to be a complete source of information on tuberculosis (TB), but rather a convenient reference for detecting and preventing TB and providing follow-up care to patients.

Since many countries in the region have similar TB control systems and guidelines, much of what is in this guide will apply to readers in all countries. However, since there are variations in policy and guidelines by country, the guide cannot reflect specific country regulations. This guide presents general principles of TB control and is not intended to contradict national guidelines. For specific details, readers should refer to their national TB control regulations. This guide may also be adapted by the National Tuberculosis Programmes of individual countries to reflect specific national guidelines.

Because the role of PHC providers will differ by country and because of the broad audience of readers, not all readers will participate in all tasks and roles described in this guide. In keeping with the coordinated approach necessary for effective TB control, the responsibility for the tasks outlined here are shared among many health care providers. Readers are encouraged to identify and use sections of this guide that assist them in their tasks and duties.

Further, to present a complete picture, this guide also includes some information on TB control that falls outside the role of PHC providers, including diagnosis and treatment regimens for TB. While these are the responsibilities of the specialized TB services within countries in the WHO European Region with a high and intermediate burden of TB, this information may still be useful for PHC providers in increasing overall knowledge about TB and providing a full picture of the effort to control TB. Where such information is included, there is a note indicating that the following section is only for information and is not the role of the PHC provider, but of the specialized TB services.

It is hoped that the information compiled in this guide will assist PHC providers in delivering high quality, effective care when detecting TB and participating in the continuation phase of treatment and thus help reduce the overall burden of tuberculosis within the WHO European Region.

The Challenge of Tuberculosis Control

Tuberculosis (TB) presents a serious threat to public health worldwide. The World Health Organization (WHO) declared TB a global emergency in 1993. TB continues to be an area of concern in the countries of eastern Europe, the Baltic States, and the Commonwealth of Independent States (CIS). To reduce this burden, a coordinated approach is required. This approach combines implementation of an internationally approved TB control strategy with health promotion, disease prevention, case detection, and patient treatment beginning at the first patient encounter. For this effort to be successful, health care professionals of different levels and at different provider settings must participate in TB control practices. Diagnosis and treatment in the mentioned areas[1] typically occur in the specialized TB services. However, through early detection and referral for treatment, health care providers who are involved in primary health care (PHC) are the frontline suppliers of care to patients and can contribute significantly to reducing the burden of TB. This role is particularly important since a delay in detecting infectious TB patients presents a threat to the surrounding community and to health care workers.

This guide will summarize:

- Significance of TB globally and within the WHO European Region
- Epidemiology of TB
- Etiology and pathogenesis of TB
- Risk factors for TB
- Symptoms of TB
- Detection and diagnosis of TB
- Treatment of TB
- The WHO recommended strategy for TB control (DOTS)
- Special situations including TB and human immunodeficiency virus (HIV), TB in prisons, TB in children and pregnant and breastfeeding women, and multidrug-resistant TB
- Role of PHC providers in TB detection, treatment and patient education.

[1] Here and further wherever "the region" is mentioned, it refers to 16 countries with the highest TB burden targeted in this guide (the Baltic States, countries of the CIS and Romania).

Primary Health Care

This guide is intended for PHC providers. This group of health care providers is particularly important in TB control, since many TB patients report first to PHC providers within the general health care services. PHC is the first level of contact for individuals, the family and community with the national health system. PHC brings health care as close as possible to where people live and work, and constitutes the first component of a continuing health care process. PHC includes at least: health education; promotion of proper nutrition; adequate supply of safe water and basic sanitation; maternal and child care, including family planning; immunization against major infectious diseases, prevention and control of locally endemic diseases; appropriate treatment of common diseases and injuries and provision of essential drugs.

PHC should be sustained by integrated, functional and mutually supportive referral systems, such as hospitals and specialized clinics for ambulatory patients. It is an essential part of the state health care system based on methods that are practical, scientifically sound and socially acceptable. PHC should be accessible to all members of the community at a cost the country and community can afford. In urban areas, PHC institutions include territorial polyclinics (for adults and children) in proximity to their residence; women's consultations, medical points at work places and emergency medical care services. In rural areas, PHC institutions include feldsher and midwife posts (FMPs), ambulatory clinics, rural hospitals, and feldsher points at work places.

Definitions

The following are the accepted definitions used by many international organizations, including WHO. There may be differences in specific definitions according to the regulations of individual countries.

Acid-fast bacilli (AFB)	Mycobacteria that remain aniline-dyed after they have been stained and washed in an acid solution; these include TB and non-TB mycobacteria; may be detected under a microscope.
Basic (first-line) TB drugs	Drugs that are most effective against the tubercle bacilli and are used in standardized chemotherapy regimens recommended by WHO. They include: isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S).
Bacille Calmette-Guerin (BCG)	Active vaccine with live attenuated *Mycobacterium bovis.*
Chemoprophylaxis	Regimen of anti-TB drugs used to prevent TB in persons not infected with TB, but who have high risk of developing TB (i.e. children or persons with HIV/AIDS living with sputum smear-positive patients).
Chemotherapy of TB	Use of an anti-TB drug combination able to kill or prevent replication of TB mycobacteria in the patient's body.
Directly Observed Treatment	A strategy of treatment in which a specifically trained health care worker observes the patient swallowing his or her anti-TB drugs.
Extrapulmonary TB	TB involving any organ other than lung parenchyma. According to WHO definitions, extrapulmonary TB also includes tuberculous pleuritis, upper respiratory TB and intrathoracic lymph node TB. A combination of pulmonary and extrapulmonary TB is classified as pulmonary TB.
Feldsher	A medical worker with secondary professional education, who has the right to provide first aid and primary health care at feldsher and midwife posts (FMPs): assistant to a doctor at primary health care institutions.
Immuno-compromised	State in which the immune system is not working properly; secondary to several causes.
Miliary TB	TB that is characterized by severe acute progression with development of shallow foci in many organs; develops due to haematogenous dissemination of the bacteria especially in patients with immunity weakened by HIV, other disease, malnutrition or old age.
Monitoring of treatment	System of uninterrupted follow-up on the process of and responses to treatment. It includes description of the therapy, treatment changes, adherence details, clinical changes, and adverse effects of drugs, as well as laboratory tests including sputum microscopy and other tests to assess treatment outcomes.

Definitions (continued)

Multidrug-resistant TB (MDR-TB)	Strains of *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, the two most efficacious anti-TB drugs.
Mycobacterium tuberculosis	Tubercle bacillus; bacteria that causes tuberculosis in humans.
National TB Control System/ National TB Programme	System of combating TB, defined by the state and based in a national network of TB facilities and general health care services, including PHC, whose policies, plans and activities are designed to achieve efficient case finding and treatment of TB patients
Notification rate	Number of new annually registered cases of disease per 100 000 population
Prevalence	Total number of persons with disease per 100 000 population at a given time
Preventive chemotherapy	Regimen of anti-TB drugs for infected persons with a high risk of developing TB who have no signs or symptoms of active disease, in order to prevent them from developing TB.
Primary health care (PHC)	The first level of contact of individuals, the family and community with the national health system. PHC brings health care as close as possible to where people live and work, and constitutes the first component of a continuing health care process.
Primary health care providers	Health workers, including physicians (therapeutists, general practitioners and family practitioners, etc.), nurses, midwives, auxiliaries and community workers trained socially and technically; who serve as frontline providers, responding to the health needs of the community at the PHC level.
Pulmonary TB	TB involving lung parenchyma. According to WHO definitions, a combination of pulmonary TB and extrapulmonary TB is diagnosed as pulmonary TB. Isolated involvement of larynx, trachea and major bronchi without lung parenchyma involvement should be classified as extrapulmonary TB.
Respirator	Special type of closely fitted mask with the capacity to filter particles one micron in size to protect the wearer from inhaling infectious droplet nuclei.
Risk factor for tuberculosis	An aspect of personal behaviour or lifestyle, an environmental exposure, or an inborn or inherited characteristic which, on the basis of epidemiological evidence, is known to be associated with TB.
Sputum smear conversion	Negative result of sputum smear microscopy at the end of the intensive phase of treatment in patients who were initially diagnosed with sputum smear-positive TB.

Definitions (continued)

Standard chemotherapy	Chemotherapy for an average of 6-8 months based on the combination of at least four major drugs (isoniazid, rifampicin, pyrazinamide and ethambutol [streptomycin]) given for 2-3 months during the initial intensive phase of treatment and followed by a combination of at least 2 drugs given for 4-6 months during the continuation phase of treatment.
Tuberculosis (TB)	Infectious disease caused by tuberculosis complex bacteria (*M. tuberculosis M. bovis, M. africanum),* which is transmitted through the air, although in extremely rare cases TB can be contracted congenitally or by drinking milk infected with *M. bovis).*
TB burden	Indicator used by WHO; number of years of healthy life that will be lost due to TB, as result of both illnesses and premature death, in a population with given, standard life expectancy by age.
WHO Strategy for Controlling Tuberculosis (DOTS)	Combination of five technical and managerial components ensuring availability of a diagnostic and treatment network easily accessible to the population and emphasizing good programme management based on accountability, supervision and quarterly evaluation of case finding and cohort analysis of treatment outcomes.

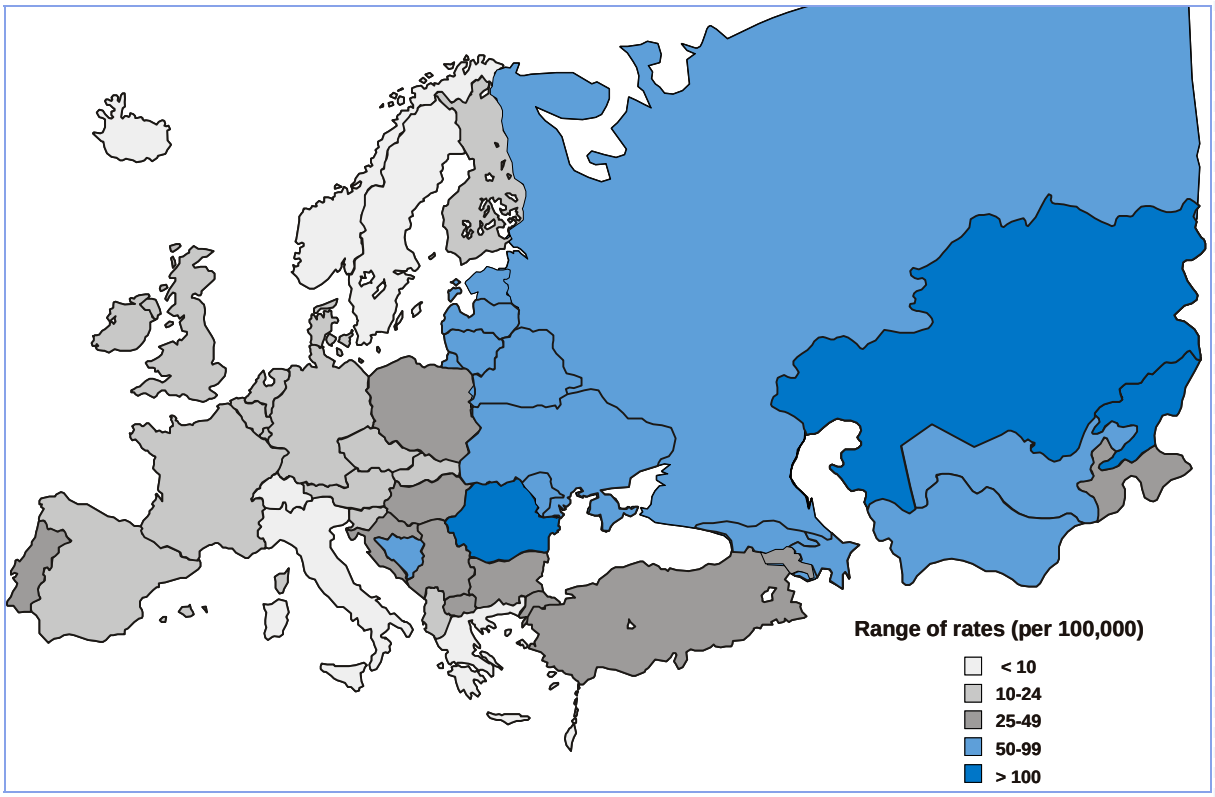
Abbreviations

AFB	Acid-fast bacilli
AIDS	Acquired immunodeficiency syndrome
BCG	Bacille Calmette-Guerin vaccine
CIS	Commonwealth of Independent States
DOTS	Internationally recommended strategy for TB control
E	Ethambutol
FMP	Feldsher and midwife post
H	Isoniazid
HIV	Human immunodeficiency virus
ITLN	Intrathoracic lymph nodes
MDR-TB	Multidrug-resistant TB
PHC	Primary health care
R	Rifampicin
S	Streptomycin
TB	Tuberculosis
TB/HIV	HIV-related TB
TST	Tuberculin skin test
UNION	International Union Against Tuberculosis and Lung Disease
WHO	World Health Organization
Z	Pyrazinamide

Global and Regional Epidemiology of Tuberculosis

About one third of the world's population is infected with *Mycobacterium tuberculosis* (*M. tuberculosis*). Each year there are an estimated 8.4 million new cases of TB and approximately 2 million deaths from the disease. *M. tuberculosis* kills more people than any other single infectious agent. TB disproportionately affects those in the economically productive age groups. In the WHO European Region, more young people and adults die from TB than any other infectious disease. The TB situation is critical in 16[1] of the 51 countries in the WHO European Region with a resurgence of the disease and a dramatic increase in notification rates in the last 10 years (Figure 1). In 2001, more than 368 000 new cases of the disease were registered in the WHO European Region; the countries of the former USSR and Romania accounted for about 80% of these new cases.

Figure 1: Tuberculosis Case Notification Rates, 2000



[1] Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan

Multidrug-Resistant Tuberculosis

Multidrug-resistant tuberculosis (MDR-TB) poses a serious threat to the maintenance of an effective TB control strategy in several countries in the WHO European Region with a high TB burden, specifically in countries that formerly were part of the USSR.

MDR-TB is caused by inadequate or incomplete treatment, which may be a result of irregular intake of anti-TB drugs or inadequate regimens. It can also be caused by an interruption in the supply of essential drugs, or by poor quality drugs. If a patient has not completed treatment successfully, or if the treatment is ineffective, he or she continues to transmit *M. tuberculosis*, which may be resistant to primary drugs. MDR-TB requires approximately two years of treatment and thus takes much longer to cure than drug-susceptible TB. Drugs to treat MDR-TB also cost more and are less effective.

Information on MDR-TB is available in Estonia, Latvia, Kazakhstan and selected oblasts of the Russian Federation and Uzbekistan. However, the true magnitude of the problem is not known in most countries of the region, because drug susceptibility testing is unavailable or cost-prohibitive in some countries with a high TB burden. Since the patients with MDR-TB from these areas are not treated with the appropriate drugs, they remain infectious and transmit drug-resistant strains of *M. tuberculosis* in the community for extended periods of time.

Tuberculosis and HIV

TB is the most common cause of death in persons with HIV infection throughout the world. HIV infection accelerates the development of TB disease due to a weakened immune system. Additionally, active TB disease further suppresses the immune systems of people living with HIV/AIDS. Thus, when a patient has a dual diagnosis of TB and HIV, both diseases progress more rapidly. The rate of TB in persons with HIV infection depends on the prevalence of TB in the region. Particular challenges can be expected in countries with a high TB burden where HIV incidence is increasing. The worsening HIV epidemic is expected to increase the TB caseload in several countries in the WHO European Region (Belarus, Estonia, Latvia, Lithuania, the Russian Federation, and Ukraine).

Tuberculosis in Special Populations

Many TB patients belong to socially vulnerable groups, including people with alcohol or drug dependence, prisoners or ex-prisoners, migrants, the unemployed, homeless persons or other at-risk populations. The process of detecting and correctly treating TB in these populations is particularly difficult; however, it is essential in preventing the spread of TB in the community.

The WHO Strategy for Tuberculosis Control (DOTS)

The tools for detecting and curing TB have been available for many years. Microscopes have been used to detect *M. tuberculosis* for more than 100 years and effective anti-TB drugs have been available for more than 50 years. Despite this, more than 2 million people worldwide die each year from TB.

The effectiveness of existing tools and approaches for controlling TB is compromised by the lack of organized health services that ensure timely detection and treatment of TB patients, particularly infectious ones. Today, however, there is a proven, cost-effective TB treatment strategy (known as DOTS), which is recommended by WHO and the International Union Against TB and Lung Disease (UNION).

The WHO TB control strategy is a combination of technical and managerial components, ensuring availability of a diagnostic and treatment network easily accessible to the population. The strategy contributes to a decrease in transmission of TB and also prevents development of drug-resistant TB, which is more expensive to cure and often fatal.

Components of the WHO Strategy for Tuberculosis Control

The WHO TB control strategy is the most effective strategy available for controlling the TB epidemic today. It has five key components:

1. **Government commitment** to sustained TB control activities at the national and regional level;
2. **Case detection by sputum smear microscopy** among symptomatic patients self-reporting to health services. Final diagnosis may be made based on sputum culture in the countries where resources are available;
3. **Standardized short-course chemotherapy treatment regimen** of an average of 6–8 months under proper case management conditions for all TB patients. This incorporates direct observation of treatment and technically sound, socially supportive treatment services;
4. **A regular quality-assured uninterrupted supply** of all essential anti-TB drugs; and
5. **A standardized recording and reporting system based on quarterly cohort analysis** that allows assessment of treatment results for each patient and of the TB control programme overall.

These components represent the minimum measures necessary to control TB. Individual countries should use the recommended strategy as a basis to establish their own national TB control programme, consistent with local circumstances and resources.

Implementation of the WHO Strategy for Tuberculosis Control in the WHO European Region

In the WHO European Region in 2002, 40 of 51 countries followed the WHO recommended TB control strategy with population coverage of 33%. The strategy has been successful in many areas of the region and has benefited countries with limited resources, as well as those in Western Europe with more developed economies such as the Netherlands, Portugal, Norway, Slovakia, Germany, Sweden and others.

2. Primary Health Care in Tuberculosis Control

In many countries of the WHO European Region, particularly in countries of the former Soviet Union, the traditionally vertically structured specialized TB care service may not coordinate fully with the PHC system. However, TB control and PHC are interdependent. Rapid progress in controlling TB will not occur in nations where TB is endemic unless TB control is integrated into the PHC system. Similarly, a PHC programme cannot be considered adequate unless it includes participation in TB control. When TB control and PHC are integrated, TB case detection and case holding can be improved and extended to benefit an entire population.

Currently, PHC providers are essential in detecting TB suspects, and referring them for treatment, thus helping to prevent spread of disease. However, the role of PHC in many countries of central and eastern Europe and the CIS is increasing. As this change occurs, the role of PHC providers in TB detection, prevention, and participation in ambulatory treatment may become even more important. To understand the current and potential role of PHC providers in TB control, it is important to understand the structure and role of the national TB control system.

Overview of National Tuberculosis Control System

The overall goals of TB control are to:

- **Reduce** mortality, morbidity and disease transmission
- **Prevent** the development of drug resistance in the community.

In countries with a high TB burden, a strong national TB control system utilizing the WHO recommended TB control strategy can be very effective in the fight against TB. In most countries of the CIS and eastern Europe, this system of national TB control services consists of a network of TB facilities, health care institutions of the Ministry of Justice, Ministry of Defense, Ministry of Railroads, and general health care services facilities, including those providing PHC.

TB control systems often follow a three-tiered structure, incorporating national, regional and district levels. The functions, roles and responsibilities of each level may vary by country according to the existing health services structure, reflecting both its population and its resources. These functions reflect the broad operational roles of TB control and define the duties of the various professionals found at each level of the TB control structure.

Role of Primary Health Care Providers in Tuberculosis Control

Although the role of PHC in TB control may differ from country to country, there are common elements, including the connection of PHC providers with the specialized TB services. Most links between PHC providers and the TB services exist at the district level. The specific relationship between PHC providers and the specialized TB services will differ by country and may be different for physicians or feldshers versus nurses. However, the general relationship between PHC providers and the TB services over the course of a patient's illness in a patient is described in Figure 2. Within a country PHC providers may have other responsibilities, such as prevention or vaccination that do not occur at the time of a patient's illness with TB. PHC providers should follow the regulations within their country.

Good communication with TB services can be very useful in detecting and treating patients with TB. Since PHC providers are the patient's first contact with medical services, the initial suspicion of TB most frequently occurs at the PHC level. When a PHC provider encounters a patient with symptoms indicating TB, he or she should examine the patient, take a medical history, and order sputum smear examination and X-ray (or refer to a provider who can carry out these steps). At this point, consultation with a specialist from the TB services, in person or by phone, is helpful for discussion of the case. If there is still suspicion of TB after the results have been received, the patient should be referred to the TB services for further examination and diagnosis.

These examinations should be performed as soon as possible, (within 2 to 3 days) to avoid the risk of TB transmission. If the case was unclear and the PHC provider does not hear back from the TB services regarding the diagnosis of the patient, the PHC provider should contact the TB services to obtain this information.

Figure 2: Relationship Between the TB Services and PHC Providers in TB Control

Course of Illness	Initial Presen-tation	Suspicion of TB: Diagnostic Tests	TB Diagnosis	Inpatient Treatment/ Intensive Phase	Outpatient Treatment/ Continuation Phase	Treatment Outcome	Follow-Up
Time		As soon as possible	Approx. 2 weeks	2-3 months	4-6 months		
Course of Medical Action	*PHC provider:* • Examine patient • Take medical history	*PHC provider:* • Order (refer for) tests[1] – 3 sputum smear examinations – X-ray – Other tests as necessary • Submit TB 05 form • Provide education to patient • Consult TB services (as needed) • Refer to TB services (based on outcome of test)	*In TB services*	*In TB services*	*Treatment by TB services* • PHC may provide directly observed treatment • Continue TB 01 form • Consult TB services (as needed) • Monitor patient	*Determined in TB services*	*In TB services or PHC as directed by national TB control system guidelines*

[1] All tests should be completed within 3 days of initial presentation

Specific responsibilities differ by country and role within PHC services, PHC providers should follow national regulations.

Generally, the intensive phase of treatment is provided in TB services. During the intensive phase of treatment, most TB patients' sputum converts to negative and thus, during the continuation phase of therapy, patients do not present great risk of infection to their contacts. At times, during the continuation phase of treatment, directly observed treatment is provided in PHC facilities under the supervision of the TB services. When this is to occur, the TB services should contact the facility approximately 2 to 3 weeks prior to the patient's discharge from the hospital to begin making arrangements.

If PHC providers are to participate in the continuation phase of treatment, then a collaborative relationship with TB services should be established and the PHC provider should communicate regularly with the specialized TB services (district TB specialist) regarding the progress of the patient and any other issues that may arise. The PHC provider should also refer the patient for sputum tests and check ups with his or her TB specialist. When treatment is complete, the PHC provider must inform the TB services and return the completed TB 01 (patient treatment card), which originated within the TB services. This collaborative relationship results in an increased level of care for the patient.

Functions of Primary Health Care Providers

PHC providers, including physicians, feldshers and nurses, are usually the first to meet a TB suspect, before diagnosis occurs. They have the unique opportunity to decrease the burden of TB through early detection since a person with active TB, who is undetected and left untreated, will infect an average of 10 to 15 other people per year.

Although the specific roles of PHC providers in TB control will differ according to individual national guidelines, PHC providers should suspect TB in patients presenting with symptoms suggestive of TB and perform (or refer for) primary evaluation and diagnosis (sputum examination and chest X-ray) to rule out the disease. PHC provider functions may include the following:

- **Suspect** TB and react quickly when patients present with symptoms suspicious of TB;
- **Ensure** collection of high quality sputum for microscopy as the basic tool for detection of TB and monitoring of treatment;
- **Ensure** that every patient with a productive cough of greater than 2 to 3 weeks has three sputum samples examined for acid-fast bacilli (AFB) in a designated laboratory;
- **Send** the collected diagnostic material for examination to a clinical diagnostic laboratory;
- **Order or refer** for X-ray examination;
- **Refer** TB suspects to the specialized TB services for diagnosis and treatment;
- **Communicate** to patients that TB is curable and emphasize the importance of regular and complete treatment in curing TB;
- **Communicate** with specialized TB services to be aware of diagnosis of patients who have been referred for diagnosis and treatment;
- **Emphasize** the importance of screening household and close contacts of smear-positive cases and ensuring that symptomatic contacts are evaluated, including tuberculin (Mantoux) skin testing in children;
- **Educate** the community about the signs and symptoms of TB and the need to seek medical care if these symptoms occur;
- **Provide** directly observed therapy to completion during the continuation phase of treatment under the supervision of the TB services;
- **Report** any default or complications in directly observed treatment to the TB services immediately;
- **Complete** all essential forms and return to the TB services;
- **Monitor** patients from risk groups for TB according to the national regulations; and
- **Perform** BCG vaccination and revaccination as well as tuberculin skin testing in children (according to national regulations).

3. Etiology and Pathogenesis of Tuberculosis

Etiology

TB is an infectious disease caused by *M. tuberculosis* complex (*M. tuberculosis* and occasionally by *M. bovis* and *M. africanum*). TB is transmitted through the air, though in extremely rare cases TB is spread congenitally, or through milk infected with *M. bovis*. Patients with pulmonary TB present the main source of TB transmission.

When a person with untreated infectious TB disease of the lungs coughs, laughs or sneezes, tiny particles containing *M. tuberculosis* are expelled into the air. These particles, about one to five microns in diameter, form **droplet nuclei** that can remain in the air up to several hours, depending on the environment. Transmission of the disease occurs when another person inhales air infected with the droplet nuclei. This generally occurs indoors, since good ventilation removes droplet nuclei from a contaminated space and direct sunlight rapidly kills *M. tuberculosis*.

Pathogenesis

Primary infection occurs on first exposure to *M. tuberculosis*. Since inhaled droplet nuclei (containing *M. tuberculosis*) are so small, they avoid the muco-ciliary defences of the bronchi and lodge in the terminal alveoli (air sacs) of the lungs. Infection begins when the bacilli start replicating in the lungs, forming the pneumonic focus. *M. tuberculosis* replicates slowly but continuously and spreads via the lymphatic system to the hilar lymph nodes. The pneumonic focus and related hilar lymphadenopathy form the primary complex. Bacilli may spread in the blood from the primary complex throughout the body of an infected person. The next phase is determined by the strength of the immune response of the infected person. In most people with competent immune systems, the immune response would stop the replication of *M. tuberculosis*; however some bacilli may remain dormant (latent infection). The immune response in a few cases is not strong enough to prevent replication of *M. tuberculosis* and primary TB disease develops within a few months. Post-primary TB may develop several years after the primary infection as a result of reactivation of a latent TB focus or re-infection (a repeat infection in a person who has already had a primary infection). In 80- 85% of cases, TB affects the lungs, although it can involve any part of the body.

Tuberculosis Infection

When a person with a competent immune system is infected with *M. tuberculosis*, the body's immune system usually responds quickly, producing lymphocytes that stop the replication and spread of the bacilli. In general, the immune response develops about 4–6 weeks after the infection. In these asymptomatic but infected individuals, the only evidence of infection may be a positive tuberculin (Mantoux) skin test, (especially in a population that has not been vaccinated with BCG). When a skin test is given to a person vaccinated with BCG, especially one who was recently vaccinated, the differential diagnosis should be done between natural TB infection and post-vaccinal response.

Risk of Infection

An individual's risk of infection depends on the concentration of *M. tuberculosis* in the air and the length of exposure to the infection (the period of inhalation of infected air), as well as on an individual's susceptibility to the infection.

If another uninfected person inhales the air containing the droplet nuclei, infection may occur. Not everyone who is exposed to an infectious TB patient becomes infected with *M. tuberculosis*. The greatest risk of infection exists when a person is continually exposed to someone within his or her household who has untreated sputum smear-positive pulmonary TB. The risk for transmitting infection from a person with sputum smear-negative pulmonary TB is low, and with extrapulmonary TB, it is even lower (almost absent). Understanding the risks for infection is essential in tracing contacts and detecting additional cases of TB.

The risk of infection depends on a variety of factors, generally increasing with:

- **Longer** exposure to infection (longer period of time breathing air shared with infectious TB patient);
- **Smaller** volume of the shared space (occupying a small enclosed space with an infectious TB patient);
- **Lack** of ventilation and direct sunlight in the common space; and

- **Higher** number of mycobacteria generated by the infectious TB patient due to:
  - Disease of the lungs, upper airways or larynx;
  - Presence of cough or other forceful expiratory measures (sneezing, singing, etc.), in particular when the patient fails to cover the mouth and nose when coughing or sneezing;
  - Presence and extent of cavitation by chest X-ray; and
  - An insufficient treatment.

The higher the AFB count, as indicated by sputum smear results, the more droplet nuclei are expelled, and the more infectious the patient.

Progression of Tuberculosis Infection to Disease

TB infection does not always lead to TB disease.

- The majority of people infected with *M. tuberculosis* (about 90%) never develop TB disease (provided their immunity is not compromised by HIV infection or other conditions).
- TB disease develops when the immune system cannot keep the *M. tuberculosis* bacilli under control, and the bacilli begin to multiply rapidly. The risk that TB disease will develop is higher in individuals with a weakened immune system (see Table 1).
- Although infected persons can develop active TB disease at any time, the risk is highest 1–2 years after a new infection and decreases as time passes. The ***lifetime*** risk of developing TB disease in infected persons with competent immune systems is **10%**.
- HIV-related decreased immunity is the most significant factor that influences the progression of TB infection to TB disease. A person infected with both HIV and TB has a **50%** ***lifetime*** risk of developing TB disease.

Risk Factors for Tuberculosis Infection and Developing Tuberculosis Disease

There are a number of known risk factors that increase the likelihood of becoming infected with *M. tuberculosis* and of developing TB disease when infected. Some of these factors may increase likelihood of both infection *and* disease.

Additionally, there are specific groups within the population that are more likely to be infected with TB and develop disease. PHC providers should consider the possible TB risk factors and risk groups as outlined in Table 1 when examining patients with symptoms suggestive of TB.

Table 1: Risk Factors for TB Infection and Developing TB Disease

Risk factors for infection	1. A continuous close contact with an infectious TB patient 2. An increased individual susceptibility to infection Risk Groups • People sharing residential accommodations with a TB patient (e.g., apartment, hostels or social care homes) • Health care personnel • Prisoners, ex-prisoners and personnel working in penal institutions • People who abuse alcohol and/or drugs • People belonging to socially vulnerable populations, such as homeless, unemployed or migrants.
Risk factors for developing TB disease	1. Presence of primary infection 2. Decreased immunity (immunodeficiency) Risk Groups • People recently infected (within the first 2 years after infection) • People with X-ray abnormalities indicating TB in the past • People with HIV infection • People who are immunocompromised due to other medical conditions (e.g., persons receiving cytostatics, radiation or corticosteroids, with diabetes mellitus or gastric and duodenal peptic ulcer) • Active smokers • People with a decreased body weight (10% or more below ideal body weight) • People who abuse alcohol and/or drugs • People belonging to socially vulnerable populations, such as the homeless, unemployed or migrants • Prisoners, ex-prisoners and personnel working in penal institutions • People sharing residential accommodations with a TB patient (e.g., apartments, hostels or social care homes).

Infection Control

Infection control procedures in health care facilities are very important to protect the health of care providers and other patients at the facility.

There are three levels of infection control measures within health care facilities: administrative (managerial); environmental; and personal respiratory protection. Each level operates at a different point in the transmission process. Administrative controls are the most important, followed by environmental controls and personal respiratory protection. Table 2 presents an overview of infection control procedures in health care facilities.

In addition to infection control within the health care facility, it is important to remember to discuss personal infection control with TB suspects, such as covering the mouth and nose when coughing or sneezing. This single step will decrease the risk of transmission. More specific information on infection control is presented throughout this guide, especially in the sections on sputum collection, and patient education. Additionally, please consult the WHO publication: *Guidelines for the Prevention of Tuberculosis in Health Care Facilities in Resource-Limited Settings* for further guidance on infection control procedures.

Table 2: Infection Control Priorities in Health Care Facilities

Priority 1 -- Administrative (Managerial) Controls: Plans and Policies

Purpose: Reduce health care provider and patient exposure by preventing droplet nuclei from being transmitted.

Actions for PHC Providers

- **Detect** potentially infectious TB patients promptly;
- **Act** quickly to separate these patients from general patient areas;
- **Refer** to the TB services to ensure prompt initiation of appropriate treatment; and
- **Follow** infection control plan of facility.

Priority 2 -- Environmental Controls: Physical Measures

Purpose: Reduce the concentration of infectious droplet nuclei.

Actions for PHC Providers

- **Maximize** natural ventilation and control direction of airflow (to draw air away from areas with people) in TB patient areas and when collecting sputum by:
  - Opening windows; and
  - Using window fans or exhaust systems in isolation rooms to draw air outside.

Priority 3 -- Personal Respiratory Protection (Respirators)

Purpose: Protect health care providers in areas where concentrations of droplet nuclei cannot be adequately reduced by administrative or environmental controls.

Actions for PHC Providers

- **Know** that:
  - Wearing a cloth or paper surgical mask **does not** protect wearer (i.e., health care workers) from inhaling infectious droplet nuclei in the air;
  - Cloth or paper surgical masks worn by an infectious patient can prevent spread of micro-organisms from the wearer to others by capturing the large wet particles near the nose and mouth;
  - Without appropriate administrative and environmental controls, respirators will NOT adequately protect health care providers from infection;
  - Respirators serve as a valuable complement to other infection controls;
- **Use** respirators on a limited basis, such as in high-risk settings including:
  - Isolation rooms for TB patients;
  - During sputum induction or other cough induction procedures;
  - Bronchoscopy suites;
  - Autopsy areas;
  - Spirometry rooms; and
  - During emergency surgery on potentially infectious TB patients.

Detecting Tuberculosis

Familiarity with TB symptoms is crucial in early detection of the disease. PHC providers must think of the possibility of TB when they encounter a patient with symptoms suggestive of TB or an abnormal chest X-ray. This is essential to initiating primary evaluation of the patient, and if the proper diagnostic tests confirm the suspicion, to referring the patient to the specialized TB services, where the TB diagnosis will be confirmed or ruled out. Other conditions that mimic TB should be ruled out as well.

Although people with TB disease can remain without symptoms, more than 90% of patients with rapidly progressive pulmonary disease have one or more clinical symptoms. These symptoms develop soon after onset of disease, prompting many people with TB to seek medical advice (often from PHC providers). TB symptoms may also be detected in patients who are unaware of the typical signs of TB and present at a general health care services facility seeking care for other conditions. PHC providers should be alert and actively question patients regarding symptoms that may be suggestive of TB.

Site of TB Disease

There are two main categories of TB, pulmonary and extrapulmonary. In general, recommended treatment regimens are similar irrespective of site. The importance of defining site is primarily for recording and reporting purposes and assessing the infectivity of the patient. According to WHO definitions:

Pulmonary TB refers to disease *involving the lung parenchyma*. Therefore tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs constitutes a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

Extrapulmonary TB refers to TB of organs other than the lungs, (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, and meninges). The definition of an extrapulmonary TB case with several sites affected depends on the site representing the most severe form of the disease. Diagnosis is based on one culture-positive specimen, or histological or strong clinical evidence consistent with active extrapulmonary TB, followed by a decision by a clinician to treat with a full course of anti-TB chemotherapy.

While diagnosis of TB within the region is made in the specialized TB services, the primary evaluation of patients presenting with symptoms suggestive of TB that lead to this diagnosis, is often performed by PHC providers. There are several elements involved in the primary evaluation and more than one type of PHC provider can contribute to a given element. Further, the role of the PHC provider within the general health care services may differ by country. As always, PHC providers should follow their national guidelines.

To conduct a primary evaluation of a patient presenting with symptoms suggestive of TB:

1. **Obtain** an accurate medical history.
2. **Complete** a physical exam.
3. **Ensure (or refer** to appropriate services for)
   - **AFB microscopy** of three good quality sputum smears; and
   - **Chest X-ray** examination.
4. **Refer** the patient to the nearest facility in which a TB diagnosis can be confirmed or ruled out.

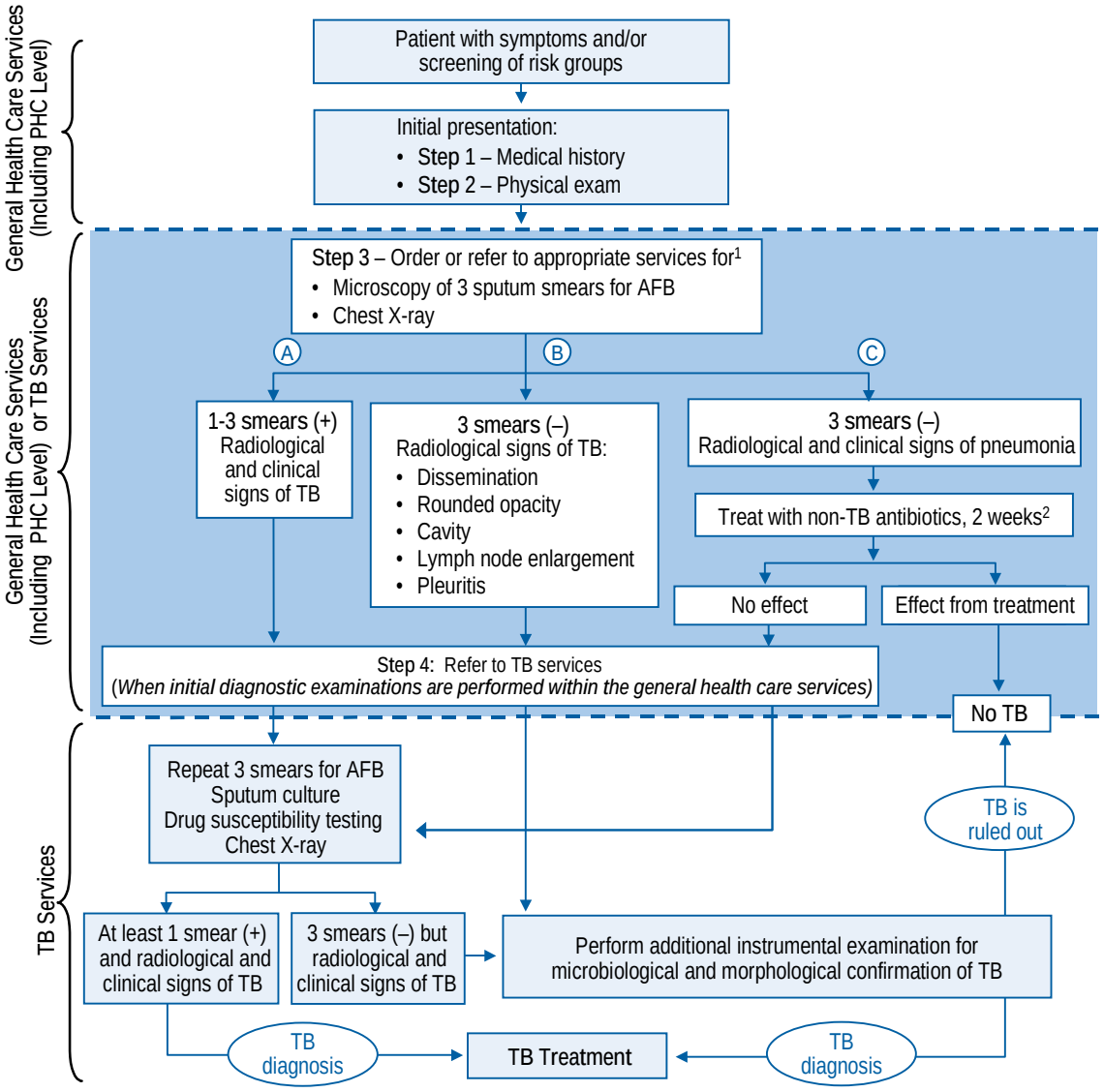
The algorithm in Figure 3 depicts additional information on the use of these steps in detecting and diagnosing pulmonary TB.

Medical History of Patient

Obtain a complete history, including social, family, medical and occupational background. Additionally, exposure to TB, symptoms of TB, history of TB and presence of risk factors for TB infection or disease are important elements in detecting TB. Table 3 presents a summary of topics that should be addressed with a patient who presents with symptoms suggestive of TB.

Figure 3: Algorithm for Detecting and Diagnosing Pulmonary TB

This algorithm presents a complete picture of all the steps in detecting and diagnosing TB. Some of the actions are performed in the specialized TB services where diagnosis should be made, but they are presented so that the full process and context of PHC activities can be seen. Additionally, the roles and responsibilities of PHC providers in TB control may differ by country, so some of the roles performed at the PHC level in one country, may be performed by the specialized TB services in another. PHC providers should follow the appropriate national guidelines.



[1] In many areas the initial sputum microscopy and X-rays, Step 3, are conducted by PHC providers within the general health care services. In other areas, these activities are conducted within TB services. Shading between the dotted lines is used to indicate areas where the responsibilities may occur either in the general health care services or the specialized TB services. Where national guidelines instruct to do so, and facilities exist, PHC providers should perform initial diagnostic tests noted in shaded areas between the dotted lines.

[2] A treatment course with broad-spectrum antibiotics should not include anti-TB drugs (including streptomycin, rifampicin, and fluoroquinalones).

Although taking a medical history is often seen as a duty of a physician, Table 3 also presents useful information for feldshers, nurses or anyone who initially speaks to the patient and records his or her complaint.

Table 3: Determining the Medical History of a TB Suspect

Symptoms of TB	*Determine if the patient has any of the following symptoms of pulmonary TB. These include:* • Respiratory symptoms: – Cough for more than 2 - 3 weeks – Chest pain – Shortness of breath – Coughing up blood • Other symptoms – Weight loss – Tiredness – Fever – Night sweats – Loss of appetite
	Determine if the patient has any general or local symptoms of extra pulmonary TB: • General symptoms of weight loss, fever or night sweats; • Local symptoms depend on the organs involved. Examples include: – Lymph node involvement: swelling, occasionally with pus drainage; – TB of the joints: pain and swelling of the joints; – Tuberculous meningitis (usually in children): headache, fever, stiffness of the neck and drowsiness; and – TB of the urinary tract: blood in the urine.
Exposure to TB	*Determine if the patient (currently or in the past) lives, works or spends time with anyone who has TB or TB symptoms.*
History of TB	*Determine if the patient has ever been diagnosed with TB infection or disease and whether he or she has taken anti-TB drugs. If the patient has a history of TB, the possibility of relapse must be considered.* • If a patient has had TB disease before, determine when and how the disease was treated. • This information will be vital for proper design of a chemotherapy regimen by a TB specialist. – Patients have a higher risk for acquired resistance to one or more of the standard anti-TB drugs. – Risk is highest if the regimen prescribed in the past was inadequate or the patient did not adhere to the recommended treatment.
Risk factors for TB disease	*Determine if the patient belongs to one or more of the groups at high risk for developing TB. See Table 1.*

Methods of Tuberculosis Detection and Diagnosis

Diagnostic Microbiology: the Principal Tool for Tuberculosis Diagnosis

The two primary methods of diagnostic microbiology available are AFB smear microscopy using the Ziehl-Neelson method and bacteriologic culture. Both methods are primarily conducted on sputum obtained from a TB suspect, although other fluid specimens, such as pus, spinal or pleural fluids can also be used.

Sputum Smear Microscopy

- AFB smear is an essential tool in controlling TB since it helps to identify the most infectious patients; those who are expelling higher numbers of *M. tuberculosis* bacilli.
- A higher AFB count indicates a larger number of bacteria present in a patient's lungs, as well as a larger number of bacteria being expelled.
- Patients with smear-positive pulmonary TB pose the greatest risk of transmission to the community.
- Sputum smear microscopy is a quick, cost-effective method to detect TB, and in some areas, it is the only microbiologic tool available.

Culture Testing

- Culture testing is not available in many areas. Although smear microscopy is an effective way to detect TB, bacteriologic culture is a more sensitive method for confirming TB diagnosis. Culture testing is usually performed by specialized bacteriological TB laboratory services.
- Once *M. tuberculosis* is identified, drug susceptibility testing can be performed to identify patients with drug-resistant strains of bacteria. Primary culture to identify *M. tuberculosis* usually takes from 4 to 6 weeks and subsequent DST usually takes an additional 4 to 6 weeks.

Collecting Sputum

Obtaining adequate sputum specimens from TB suspects is essential in TB diagnosis. Always collect three separate sputum specimens for microscopic examination for AFB in all patients in which evidence suggests TB (e.g., long duration of productive cough), **even in those with normal chest X-rays.**

Sputum specimens:

- Should be collected within 2 days of clinical assessment (according to the methods listed in Table 4) to reduce the number of clinic visits by a patient. Method 1 is preferred.
- Should include:
  - Two "spot" sputum samples collected during the patient's visits to the clinic under the direct supervision of a health care worker;
  - One sample collected at the patient's home *early in the morning prior to eating, but after cleaning teeth* (to obtain a sample that is not contaminated with food).
- Should consist of good quality sputum (not saliva) in order to be useful for sputum smear microscopy. Good quality sputum:
  - Is frequently thick and mucoid;
  - May be fluid with chunks of dead tissue; and
  - May range in color from opaque white to green (bloody specimens will be reddish brown).

Table 4: Sputum Collection Schedules

Method 1	
1st Sputum Sample (DAY 1)	PHC provider should: • Directly supervise collection of the first specimen when a patient suspected of TB visits the clinic for the first time; • Instruct the patient on necessity of collecting 3 specimens of sputum and describe sputum collection in home conditions; • Give the patient a sputum container and direct the patient to use it in collecting a specimen the next morning at home and to return the specimen to the clinic; and • Write a specimen identification number on the external surface of the sputum container (not on the lid).
2nd Sputum Sample (DAY 2)	Patient should: • Cough up the second sputum sample into the collection container upon waking the following morning (*early in the morning, prior to eating but after brushing the teeth), and* • Bring the specimen back to the clinic as soon as possible.
3rd Sputum Sample (DAY 2)	PHC provider should: • Directly supervise collection of the third specimen when the patient returns to the clinic with the second specimen collected at home that morning.
Method 2	
1st Sputum Sample (DAY 1)	PHC provider should: • Directly supervise collection of the first specimen when a patient, suspected of TB visits the clinic for the first time; • Instruct the patient on necessity of collecting three specimens of sputum; • Write a specimen identification number on the external surface of the sputum container (not on the lid); and • Instruct the patient to proceed to the appropriate location within the clinic or hospital for further diagnostic tests (e.g. X-rays) and to return following those tests.
2nd Sputum Sample (DAY 1)	PHC provider should: • Directly supervise collection of the second specimen when the TB suspect returns from the other diagnostic tests within the hospital or clinic; • Describe the process of sputum collection in home conditions; • Give the patient a sputum container and direct the patient to use it in collecting a specimen the next morning at home and to return the specimen to the clinic; and • Write a specimen identification number on the external surface of the sputum container (not on the lid).
3rd Sputum Sample (DAY 2)	Patient should: • Cough up the third sputum specimen into the collection container upon waking the following morning (*early in the morning prior to eating but after brushing the teeth); and* • Bring the specimen back to the clinic as soon as possible.

Table 5 reviews sputum collection procedures, which will produce adequate sputum specimens from TB suspects.

Table 5: Sputum Collection Procedures

Setting	Sputum Containers
Follow these guidelines in **health care facilities**. • Use properly ventilated, designated sputum collection rooms (used for this purpose only) to collect sputum. • Collect sputum in a specially designated room with open windows, (in winter with one window frame open) or outside in the open air in the absence of a sputum collection room. • Mark sputum collection rooms to warn other patients and family members not to enter the room and to remind attending staff that respiratory protection should be worn. • Store sputum in a cool place until it is sent for microscopy. Ideally sputum should be stored in a refrigerator (separate from food). Sputum may be stored for up to one week, although it should be sent to the laboratory as soon as possible. Follow these guidelines in **the patient's home**. • Instruct patient to collect sputum outdoors in the open air or indoors away from other people and in front of an open window. • Instruct the patient to bring the sample to the clinic as soon as possible after collection.	Robust, leak-proof and clean sputum collection containers are essential. Recommended containers are: • Wide-mouthed (approximately 35 mm in diameter) • Transparent • Durable • Able to be closed tightly • Easily labelled on outer surface • Clean and preferably sterile • Made of single-use combustible materials (if resources permit) • If reusable, typically made of heavy glass with a screw-cap top Clean and sterilize reusable containers by boiling in water with soap, other detergent or other disinfectant for at least 30 minutes. Then, rinse thoroughly with clean water and sterilize in a dry oven.
Health Care Worker Safety	**Patient Education and Instructions**
Take appropriate infection-control precautions when supervising patients who are producing sputum. • Use a respirator and rubber gloves. • Stand behind the patient or, if possible, leave the room when the patient coughs up sputum and observe through a door with a glass window.	To help the patient collect quality sputum sample, describe in detail why and how to collect sputum so that the patient will know what to expect and what actions to take. To assist patients in producing an adequate sputum sample: • Explain the process of correct sputum collection; • Provide thorough education; • Demonstrate proper techniques (see the following section); and • Provide encouragement and support.

Instructions for Producing an Adequate Sputum Specimen

Instruct the patient on production of an adequate sputum sample using the steps below. Figure 4 can be used to teach the patient how to produce sputum.

- **Rinse mouth** with water before producing sputum to help remove food and any contaminating bacteria in the mouth (except for early morning sample, collected at home by patient).
- **Take two deep breaths**, holding the breath for a few seconds after each inhalation and then exhaling slowly. Breathe a third time and then forcefully blow (exhale) the air. Breathe in again and cough from deep within the lungs.
- **Hold the container** close to the lips and spit into it gently after a productive cough.
- **Tightly secure** the lid on the collection bottle.
- **Wash hands** with soap and water.

Request for Sputum Microscopy Examination Form (TB 05)

After all three sputum specimens are collected, label the containers (not the lids) with the appropriate patient identifier and send them to the laboratory for acid-fast smear microscopy examination.

- **Fill out** the top half of the Request for Sputum Microscopy Examination form, TB 05, (Annex 1A).
- **Include the form** with all three of the patient's sputum samples. (Fill out only one form for all three sputum specimens collected from a patient.)
- **Pack form** with a patient's sputum specimens for transport to the designated microscopy laboratory for examination.

The "Results" section, on the bottom half of the form, will be completed by the microscopy laboratory after the sputum specimens are examined.

Figure 4: Correct Sputum Collection

Modified from Tomsk Oblast TB Dispensary/Merlin poster

The Chest X-Ray

The chest X-ray is another tool used in diagnosing TB. The chest X-ray:

- Helps in diagnosing TB disease, since about 80 to 85% of TB patients have pulmonary TB;
- Usually appears abnormal in a person with pulmonary TB disease; and
- Is **unreliable** for diagnosis **when considered alone** because other chest diseases can resemble TB on a chest X-ray, and there is no radiographic pattern that is absolutely typical of pulmonary TB.

Although an abnormality on a chest X-ray may lead a clinician to suspect TB, it is important to bear in mind that ***the results of a chest X-ray alone cannot confirm diagnosis of TB disease.*** Old healed scars from appropriately treated TB can cause abnormalities, but these may be unrelated to disease or relapse.

In some countries, fluorography has been widely used as a screening method for the general healthy population. However, since fluorography is also prohibitively expensive, its use results in resources being diverted from medication and treatment of patients with active TB disease. For these reasons, fluorography is not recommended for the general population. Instead, targeted screening of groups with specific risk factors for TB (described in Section 3) is recommended for use as a detection method in countries with high prevalence of TB.

If sputum collection/microscopy or radiology is not available at a PHC facility, the patient must be referred to a health care institution equipped with these diagnostic tools. To avoid transmission of TB, try to arrange special transportation for the patient. If special transportation is not possible, first try to make arrangements to collect and send three sputum samples from the patient to the appropriate facility, rather than sending the patient by public transportation.

Tuberculin (Mantoux) Skin Test

Mantoux skin tests are mostly used as a diagnostic tool in detecting TB in children. Further discussion is included in Section 6, Special Situations: TB in Children.

Classification of Tuberculosis Cases

Although diagnosis of TB and classification of TB cases currently occur in the specialized TB services, it may be useful for PHC providers to be familiar with these terms. This is particularly important when directly observed treatment during the continuation phase is provided in the general health care services at the PHC level, under the supervision of the specialized TB services.

According to WHO recommendations, every TB patient is classified within a specific diagnostic category and the corresponding treatment regimen for that diagnostic category should be administered. Classification occurs within the TB services and is based on the following determinants:

1. Site of disease
2. Bacteriology
3. History of previously treated TB
4. Severity.

Classification of TB cases is useful for a number of reasons, as it:

- **Ensures** proper patient registration and case notification;
- **Allows** prioritising of treatment for sputum-smear positive cases, the main sources of infection in the community;
- **Allocates** cases to appropriate standardized treatment regimens;
- **Assists** in evaluating the proportion of cases according to organ, bacteriology, and history of previous treatment for TB; and
- **Assists** in evaluating treatment outcomes using cohort analysis.

For background information, a summary of the system of classification of TB cases can be seen in Annex 2A, Classification of TB Cases.

Standardized Chemotherapy

WHO and the UNION recommend specific standardized chemotherapy regimens for treatment of TB. These standardized regimens allow for provision of effective treatment and prevent the development of MDR-TB. Every treatment regimen for TB has a standard code, and each anti-TB drug has a standard abbreviation as seen below:

- Isoniazid (H)
- Rifampicin (R)
- Pyrazinamide (Z)
- Ethambutol (E)
- Streptomycin (S)

Although TB treatment is initiated within the specialized TB services in countries in the WHO European Region, further information on dose form, strength and recommended dosage for anti-TB drugs can be seen in Annex 2B.This table may be helpful for PHC providers who are participating in the continuation phase of treatment.

A TB treatment regimen consists of two phases:

Intensive Phase: First phase of TB treatment (for 2-3 months) with 4 to 5 essential anti-TB drugs, following a selected treatment regimen, to rapidly kill *M. tuberculosis* bacilli, prevent selection of resistant *M. tuberculosis* and stop infectiousness. Directly observed treatment is crucial to ensure that the TB patient takes every prescribed dose of medicine. This phase is generally administered on an inpatient basis in a specialized TB facility (but can also be provided in an outpatient setting).

Continuation Phase: Second phase of TB treatment (with fewer drugs than the intensive phase according to the treatment regimen) to kill semi-dormant *M. tuberculosis* bacilli and sterilize the lesion. This phase is generally administered on an outpatient basis. Since the patient may be feeling better, and it is more difficult to ensure proper treatment control for a variety of reasons, there is a higher risk of interruption during this phase.

The regimen recommended for each patient depends on the diagnostic category for that patient. Although physicians in the specialized TB services select the appropriate regimen, a brief overview of treatment regimens and drugs may be useful for PHC physicians and other providers, particularly if they are involved in delivering directly observed treatment during the continuation phase of therapy. For informational purposes, these regimens are shown in Annex 2C, Recommended Treatment Regimen for Each Diagnostic Category.

There are different practices for chemoprophylaxis within the WHO European Region. PHC providers should follow national guidelines on chemoprophylaxis or preventive chemotherapy for both children and adults.

Directly Observed Treatment

Directly observed standard treatment is an important element of the WHO strategy. In directly observed treatment, a health care worker watches the patient swallow his or her anti-TB drugs, ensuring that the patient is taking the drugs correctly. Directly observed treatment:

- **Can be administered** in hospitals, sanatoria or outpatient settings;
- **Can be observed** by TB specialists (district TB doctor), PHC providers, (physician, nurse or feldsher) or representatives from the Red Cross or other humanitarian organizations. Directly observed treatment by a family member is not encouraged due to the complex interpersonal family relationships that may affect acceptance or adherence (however family support and encouragement in emphasizing the importance of completing treatment is very significant); and
- **May include** incentives (such as food or transportation) for the adherent patient and/or the health care worker who supervises directly observed treatment. This can increase motivation for both the patient and the supervisor.

Participation in Tuberculosis Treatment by Primary Health Care Providers

Most patients receive the intensive phase of directly observed treatment in an inpatient setting at the specialized TB services. After adequate therapy in the intensive phase, most patients have become non-infectious and can be discharged from the hospital to continue treatment on an ambulatory basis. Directly observed treatment is a key element during this phase. A TB patient who must travel far for treatment is less likely to be adherent. Because of this, the TB services often try to coordinate directly observed TB treatment as close to the patient's home (or sometimes the workplace) as possible. This coordination needs the involvement of PHC facilities (polyclinics, FMPs, rural hospitals, etc.), which are located close to the TB patient's home. In these cases, treatment decisions are still made within the TB services and PHC providers should consult the TB services regularly regarding the progress of the patient and any problems that may occur.

In some cases, a physician from the specialized TB services or the general health care services may provide directly observed treatment. However, most of the time, the treatment supervisor (observer) will be a medical nurse, feldsher or Red Cross/Red Crescent nurse. PHC providers with patients who are receiving directly observed treatment should:

- **Fill in the TB 01 Patient Treatment Card** (Annex 1B), (originated in TB Service) when treatment is observed;
- **Stay in regular contact** with the district TB specialist, or appropriate physician within the TB services;
- **Be aware** of any problems that may occur and report them to the appropriate TB services physician immediately;
- **Verify that** drugs from TB services are received on time to ensure that drugs are available to complete the full course of treatment without interruption. (Anti-TB drugs, like most medications, should be stored in a cool dry place, tightly sealed, and away from sunlight and heat); and
- **Discuss** importance of adherence with the patient.

Further information on improving adherence can be found in Section 8, Adherence to Treatment.

Monitoring of Treatment

Regular monitoring by the TB services is necessary to determine the progress and outcome of TB treatment. Monitoring treatment is one of the most important elements of an effective TB control programme. Treatment monitoring can help assess:

- **Whether** a patient is becoming more or less infectious
- **How** a patient is progressing clinically
- **When** treatment is complete
- **Potential** adverse effects of anti-TB drugs.

Treatment monitoring is a priority for the specialized TB services. However PHC providers may also play an important role in monitoring activities. Monitoring requires a close level of cooperation with local TB services. PHC providers:

- Conduct direct observation how patients when they swallow anti-TB drugs during the treatment period;
- Check for development of adverse reactions to drugs;
- Refer TB patients for regular visits to a TB specialist for monitoring purposes;
- Consult TB services regularly regarding progress of patient and any problems that occur; and
- Order sputum microscopy examination during the treatment period.
  - As with the initial sputum collection, appropriate procedures should be followed, and a TB 05 (Annex 1A) form completed and sent to the lab.
  - Monitoring schedules differ based on the category to which the patient is assigned, and the results of sputum analysis. Follow the direction of the TB services in collecting sputum for monitoring.

When treatment is completed, outcomes are determined by the specialized TB services. However, for general information, a review of treatment outcome definitions can be found in Annex 2D.

Adverse Effects

Symptom-Based Approach to Adverse Effects of Anti-TB Drugs

PHC providers involved in the continuation phase of therapy should:

- **Be aware** of the potential adverse effects of the anti-TB drugs;
- **Monitor** patient for dangerous reactions;
- **Teach** patient how to recognize any adverse effects and report them, but reassure patient that adverse effects to the drugs are rare; and
- **Provide** encouragement and reassurance to patient and family members.

Table 6 provides guidance on a symptom-based approach to monitoring anti-TB drugs, and the correct clinical response to side effects. Adverse effects can be classified as minor or major and in most instances should be treated as follows:

- **Minor adverse effects:** Immediately inform the district TB specialist and agree on a plan for management. Provide encouragement to the patient. Generally there is no need to discontinue TB treatment.
- **Major adverse effects:** Immediately stop treatment with suspected causal medicine and inform the TB services. Refer the patient to the district TB doctor immediately (and send to emergency services if necessary).

Table 6: Overview of Adverse Effects and Their Management

Minor Adverse Effects			
Signs and Symptoms	Adverse Reaction	Caused by	Management
Orange urine, sweat, or tears Permanently stained soft contact lenses	Discoloration of body fluids	Rifampicin	• Immediately inform the district TB specialist about the reported adverse effects • Give recommendations to address side effects (agreed with the district TB specialist) such as not wearing soft contact lenses, using alternate methods of birth control, and wearing sunscreen or avoiding exposure to the sun. • Reassure the patient that this adverse effect occurs at times, and treatment should continue.
Interferes with certain medications, such as birth control pills, birth control implants, and methadone treatment	Drug interaction	Rifampicin	
Frequent sunburn	Sensitivity to the sun	Rifampicin	

Table 6: Overview of Adverse Effects and Their Management (continued)

Major Adverse Effects			
Signs and Symptoms	Adverse Reaction	Caused by	Management
Skin rash	Allergic	Any drug	• Immediately stop the suspected causal anti-TB drugs and inform the district TB specialist • Immediately refer the patient to TB services (and send to emergency services if necessary)
Blurred or changed vision Changed color vision	Eye damage	Ethambutol	
Abdominal pain Abnormal liver function test results Dark urine Fatigue Fever for 3 or more days Flu like symptoms Lack of appetite Nausea Vomiting Yellowish skin or eyes	Hepatitis	Isoniazid Pyrazinamide Rifampicin	
Dizziness Tingling or numbness around the mouth	Nervous system damage	Isoniazid	
Tingling sensation in hands and feet	Peripheral neuropathy		
Stomach upset, vomiting, lack of appetite	Upset stomach	Pyrazinamide	
Abnormal uric acid level Joint aches	Increased uric acid		
Easy bruising Slow blood clotting	Bleeding problems	Rifampicin	
Balance problems Hearing loss Ringing in the ears	Ear damage	Streptomycin	
Abnormal kidney function test results	Kidney damage		

HIV and Tuberculosis

Although the principles of the WHO strategy for TB control are the same in HIV-positive and HIV-negative patients, HIV is the most powerful factor known to increase the risk of TB. PHC providers must be alert to the possibility of TB infection in HIV-positive patients, as HIV both increases a person's susceptibility to infection with *M. tuberculosis* and is a significant cause of progression from TB infection to TB disease.

In some countries persons with HIV/AIDS are seen in specialized services. However, PHC providers who do see HIV-positive patients or patients at risk for HIV should:

- **Educate** the patient about the symptoms of TB and HIV, the risks of infection and how to prevent transmission;
- **Be aware** of the common forms and presentations of TB/HIV patients, including pulmonary, disseminated and extrapulmonary forms;
- **Ensure (**or refer to appropriate services for) AFB microscopy of three good quality sputum smears at a designated laboratory when TB is suspected and refer the patient to TB services for differential diagnosis, if necessary. (Distinguishing pulmonary TB from other HIV-related pulmonary diseases is a common diagnostic problem); and
- **Refer** patient for voluntary counselling and testing for HIV.

HIV Infection in Tuberculosis Patients

Patients diagnosed with TB will be under the care of the specialized TB services, at the least during the intensive phase. However, a PHC provider who takes care of TB patients transferred for the continuation phase of therapy should discuss HIV antibody testing with these patients. Confidential counselling is essential before and after HIV antibody testing according to the national regulations. The patient must give explicit informed consent to have the test.

More information on the clinical signs and symptoms of HIV infection in TB patients is available in the WHO publication, *TB/HIV: A Clinical Manual*.

Tuberculosis in Prisons

TB in prisons and detention centres is a severe problem in the WHO European Region. The rate of TB disease in prisons is well above the rate in the general population. In some countries, the rate of active TB among prisoners is estimated to be as high as 10%. A significant MDR-TB problem also exists in prisons.

It is essential that prisoners with active TB, who are released from prisons or detention centres, continue the full course of treatment to discourage the emergence of drug-resistant strains and the spread of TB within the community.

In some areas, PHC facilities are notified by the TB services when a prisoner with active TB is released and settles in their area. TB services may ask PHC providers within these facilities for assistance in locating the patient and ensuring that treatment is continued and completed. In some countries or regions, there are designated social nurses or social workers who can assist in this process. PHC providers who are requested to provide assistance with former prisoners on TB treatment should:

- **Ensure** that necessary medical records are received;
- **Attempt** to locate the patient using other PHC workers, or social nurses or social workers where available;
- **Use** the education/communication techniques in sections 7 and 8 to maximize adherence to the anti-TB regimen; and
- **Provide** feedback to the relevant TB services.

Tuberculosis in Children

Diagnosis of TB in children is difficult, as fewer than half the children with TB have symptoms suggestive of the disease. This is especially true in malnourished children. PHC providers must be aware of the risks for TB in children, and the symptoms that do occur.

Clinical Presentation and Detection

When a child presents with symptoms suggestive of TB, it is essential to use all available diagnostic tools and to refer the child to the TB services. The table below summarizes the tools used in detecting TB in children, as well as the information needed and actions to be taken.

Common Manifestations of Tuberculosis in Children

- Up to age two, blood-borne spread of the more fatal forms of TB is common (miliary, meningitis). After puberty, pulmonary TB is more common.
- Malnourished children of any age may develop severe TB.

Table 7: Use of Diagnostic Tools to Detect TB in Children

Clinical history and physical findings	• Assess child for presence of the following general symptoms: – Anorexia – Fever – Weight loss – Lassitude – Cough • Assess child for presence of the following local symptoms of organ involvement suggestive of extra pulmonary TB: – Enlargement of lymph nodes – Angle deformity of spine – Central nervous system symptoms – Joint or bone swelling – Abdominal mass or ascites • Refer to TB services immediately, in the presence of the following features that indicate a high likelihood of TB: – Duration of symptoms for > 4 weeks; – Weight loss to 60% of ideal body weight without improvement for 4 weeks; and – Fever not responding to routine antibacterial treatment.
History of TB exposure	• Assess for a history of contact with a TB case and inquire about symptom history of these contacts. This increases possibility that child has TB and may help identify a previously undiagnosed infectious adult case. • If child is a contact of a past or active TB case, inquire regarding treatment details of case, including treatment, drug sensitivity, adherence and follow-up.
Tuberculin skin test (TST) (Mantoux test)	• Administer tuberculin skin test: – A positive skin test does not indicate presence or extent of TB disease; it only indicates infection or post-vaccinal response. – The TST is less likely to be positive in a child who has been recently exposed to TB, or has severe malnutrition, HIV infection or disseminated TB. – Reading and interpretation of results of TST are performed in conformity with the regulatory documents of each country and depend on types of tuberculin that are used.

Table 7: Use of Diagnostic Tools to Detect TB in Children (continued)

Chest X-ray	• Order X-ray. The most common chest X-ray features of primary TB are: – Intrathoracic lymphadenopathy (hilar and right paratracheal region enlargement are the prevailing forms) – Segmental collapse – Lobar consolidation – Pleural effusion – Miliary shadows dotted through lungs in miliary TB (may not be obvious in early stages).
Specimen Exam-initiation (If specially indicated)	• Collect sputum (may be problematic as infants and young children often swallow their sputum). • Use or refer for gastric lavage and laryngeal swab when obtaining sputum is impossible (perform immediately on waking). • Use inhalation of nebulized, superheated saline via mask or tent for 15 minutes to enhance sputum collection in older children. • Collect samples from other body sites as dictated by clinical situation.

Tuberculosis Treatment in Children

Anti-TB chemotherapy is well tolerated by children and teenagers. Categories of TB treatment are similar to those for adults. Once TB has been diagnosed, the TB specialist will determine the appropriate regimen.

Tuberculosis Prevention in Children

Many countries in the WHO European Region use BCG vaccine. BCG:

- **Consists of** live attenuated strain of bovine TB bacilli that are nonvirulent (*M. bovis BCG*);
- **Is given by** intradermal injection and stimulates immunity;
- **Is recommended by** WHO to be given to newborns to prevent them from developing severe forms of TB. Revaccination is recommended in some countries, and National Ministries of Health decide on BCG vaccination and revaccination schedules. Consult and follow national regulations for specific guidance on revaccination. Since there is a lack of evidence indicating that repeat BCG immunization is effective in preventing TB in adults, WHO does not recommend revaccination; and
- **Should be administered** where the M. Deltoideus is attached to the upper arm (approximately 5 cm below the shoulder).

Active contact tracing of all children who are household contacts of smear-positive pulmonary TB cases is recommended. Screening should include:

- Taking a thorough history
- Clinical exam
- Tuberculin skin test
- Chest X-ray.

National guidelines on preventive chemotherapy and chemoprophylaxis differ within the WHO European Region. PHC providers should follow the national regulations regarding preventive chemotherapy and chemoprophylaxis regimens, where they exist. This will significantly reduce the possibility of the child developing TB disease. WHO recommends prophylaxis (isoniazid 5 mg/kg daily) for six months in asymptomatic children under five years who are household contacts of smear-positive pulmonary TB patients.

Tuberculosis in Pregnant and Breastfeeding Women

Identifying TB disease early in pregnant women is important to avoid congenital forms of TB and also to prevent airborne transmission to the infant after birth. Mothers with suspected TB should be counselled to cover their nose and mouth when coughing, especially while breastfeeding. Although all diagnostic tests for TB can mainly be performed safely on pregnant and breastfeeding women, PHC providers should always inquire whether a woman is pregnant before referring her for X-rays. When it is necessary to obtain an X-ray from a pregnant woman, abdominal shields should be used.

Even though anti-TB regimens for mother and child will be selected within the specialized TB services, the following information on use of anti-TB drugs during pregnancy is provided as background for PHC providers. In principle, most first-line anti-TB drugs (rifampicin, isoniazid, pyrazinamide and ethambutol) can be used safely during pregnancy and while breastfeeding. Although the safety of pyrazinamide in pregnancy has not been established, whenever possible the six-month regimen based on isoniazid, rifampicin and pyrazinamide should be used during pregnancy. When pyrazinamide is used, Vitamin K should be administered to the infant at birth due to the risk of postnatal haemorrhage.

Women of childbearing age should be asked whether they are pregnant before starting TB treatment, since streptomycin crosses the placenta and can cause auditory nerve impairment and nephrotoxicity to the foetus. Streptomycin

should not be used during pregnancy; however it may be used safely during breastfeeding. If a fourth drug is needed during the intensive phase for a pregnant woman, ethambutol should be used rather than streptomycin. Active TB in pregnancy must be treated because untreated disease will harm the mother and the unborn child more than the standard drugs would. All medical workers, including PHC providers, should advise pregnant women with TB that successful treatment is important for successful outcome of the pregnancy.

Infants of women with TB should be carefully managed by the TB services through chemoprophylaxis and BCG vaccination, according to national regulations. Breastfeeding children of a sputum smear-positive mother are the most important group to target for chemoprophylaxis. WHO recommends that these infants be given prophylactic isoniazid for at least 3 months beyond the time that the mother is considered non-infectious. BCG vaccination should be postponed until the end of the isoniazid prophylaxis.

Multi-Drug Resistant Tuberculosis (MDR-TB)

MDR-TB is defined as active TB with bacilli resistant at least to both rifampicin and isoniazid. MDR-TB can pose a serious threat to the community and maintenance of an effective TB control programme. Since diagnosis of MDR-TB can be difficult, undiagnosed patients remain the source of drug-resistant bacteria for prolonged periods of time, transmitting MDR-TB into the community.

MDR-TB results from incomplete, inadequate or irregular treatment. The most important cause of clinically significant drug resistance is a failure of medical practice, either to prescribe appropriate therapy or to directly observe treatment. Other causes include an interruption in drug supply or poor quality drugs. Some patients develop MDR-TB through one of the pathways noted above. Others are directly infected with MDR-TB through exposure to a person with infectious MDR-TB.

When a patient defaults from treatment, there is significant risk that drug resistant TB will develop. Following the WHO recommended TB control strategy, including standardized regimens and directly observed therapy will greatly decrease this risk.

Patients with drug-resistant TB should be treated in specialized MDR-TB units.

Since the majority of TB patients first present to general health care services, PHC providers have an opportunity to set the tone for the patient's interaction with the medical establishment. Due to the length of treatment, it can be challenging to gain a patient's commitment to curing TB. However, the PHC provider can begin to encourage commitment at the first point of encounter, when the patient is identified as a TB suspect.

When discussing the possibility of TB, it is important to be empathetic and encouraging, particularly by emphasizing that TB is curable with the proper drugs, taken in the proper way.

In addition to the above, several other techniques may be helpful for PHC providers:

- **Learn** about the patient's family and social situation.
- **Educate** the whole family in understanding the transmission of the disease, the importance of anti-TB drugs and how drug resistance occurs. Family cooperation and support have been shown to assist the patient with adherence.
- **Provide** written or other resource information to the patient, in addition to person-to-person education.
- **Continue** education for the patient throughout the entire course of treatment.
- **Reinforce** key messages throughout the patient's treatment, both to the patient and to family members. Unless the patient understands the importance of the anti-TB drugs, he or she is unlikely to adhere to the treatment prescribed. Help the patient understand:
  - How TB is spread;
  - How to stop spread of the disease (by covering his or her mouth when coughing, and by completing treatment);
  - Why many drugs must be taken;
  - That all doses of each drug must be taken;
  - That the drugs must be taken for the time prescribed, even, and especially, if he/she is feeling better;
  - The basics of drug resistance and how it occurs;
  - Why close supervision is important; and
  - The possible adverse effects of the drugs and which adverse effects should be reported *immediately*.

Effective Communication Techniques

There are a number of effective techniques that encourage free communication and involvement from the patient. Some techniques of effective communication include asking questions, listening carefully, trying to understand a patient's worries or needs, demonstrating a caring attitude and helping to solve the disease-related problems. These techniques may also be helpful in communicating with the family of the patient.

Table 8: Effective Communication Techniques

Technique	Reason	Example
Ask questions and listen.	• Assess the patient's knowledge about TB, and commitment and motivation level for treatment.	• How are you feeling? • What do you think causes TB?
Make interactions with the patient a positive experience. • Be positive and encouraging. • Demonstrate a caring and respectful attitude. • Build a sense of trust.	• Motivate patient to continue seeking care and completing treatment. • Encourage a trusting and open relationship with the patient.	• Greet patients by name; tell them that they are doing the right thing by seeking or continuing care. • Use body language, tone of voice, eye contact etc. • Display empathy and try to be helpful when the patient mentions a problem. • Be honest with the patient. • Follow-up with things you have said you will do or provide.
Communicate clearly and simply.	Ensure that: ▪ The patient understands and remembers important messages about TB and treatment; • The patient knows what to do next; and • Any fears or concerns are addressed.	• Use simple non-medical terms such as "TB germs" instead of *"Mycobacterium tuberculosis."* (If you do not, you may lose an opportunity to educate the patient and discourage them from coming back). • Use appropriate methods: If patients have difficulty reading, give instructions orally as needed and use other techniques, such as marking appointments on a calendar.

Table 8: Effective Communication Techniques (continued)

Technique	Reason	Example
Limit the amount of information.	Ensure that: • The patient understands and remembers important messages about TB and treatment; • The patient knows what to do next; and • Any fears or concerns are addressed.	• Provide essential information, and schedule another meeting, if necessary. It may be difficult for patients who are feeling sick or afraid to understand or remember everything you are saying.
Discuss the most important topics first and last.		• Select the most important message (i.e., I know you are feeling better but to get well, you must come in for all of your appointments to take your medicine). • Begin with this message and repeat it at the end.
Repeat important information.		• Repeat key messages, using comments, like, "As we discussed last time."
Use concrete examples.		• Demonstrate skills such as how to collect sputum, or how to crush a pill and mix into food. Some people may learn more effectively this way.
Encourage patient to ask questions.		• Pause frequently to ask if a patient has questions. • Praise questions when asked, by using comments such as, "Good question".
Ask questions to check the patient's understanding.		• Ask questions such as "Where will you cough up the sputum?" that require the patient to repeat information and demonstrate understanding.

For further information on patient education, please consult Module 11 - Patient Education of the WHO training modules, *Managing TB at the Raion Level.*

8. Adherence to Treatment

A relationship of trust and confidence between the TB patient and PHC providers can help promote adherence to treatment. For adherence to occur the patient and his or her family members must understand basic information about TB, including what is necessary for treatment and cure. Patient counselling and education are integral parts of the treatment process.

PHC providers and all others who interact with the patient should:

- **Be polite**, considerate and respectful;
- **Treat** the patient with dignity; and
- **Provide** the patient with an opportunity to voice concerns and ask questions regularly.

Adherence: Barriers and Strategies

Most patients respond to the concern shown by the individual who is providing their treatment **and** the importance that the provider attaches to the patient's adherence to the medication regimen.

Table 9 presents a variety of patient education techniques that can be used to address some of the underlying reasons why patients could be having difficulty completing treatment.

Table 9: Actions to Improve Patient Adherence

Reason for Poor Adherence	Potential Action by PHC Staff
Alcohol or drug abuse	• Refer patient to appropriate services, if available. • Involve patient's family in trying to encourage adherence to treatment. • Provide encouragement and reassurance and emphasize importance of treatment. • Offer incentives if available.
Stigma (fear or unwillingness to be seen as TB patient)	• Emphasize that anyone can get TB. • Emphasize TB is curable and that once treatment is initiated, most patients quickly become non-infectious. • Reassure patient that you will maintain confidentiality. • Inform patient about regulations that protect TB patients from discrimination or job loss (If such regulations exist nationally).
No longer feels sick	• Reiterate importance of completing regimen and consequences of incomplete treatment.

Table 9: Actions to Improve Patient Adherence (continued)

Reason for Poor Adherence	Potential Action by PHC Staff
Does not understand the regimen	• Explain again, involve family or set up a system to assist the patient with the regimen/schedule.
Strong personal or cultural beliefs or is using alternative regimens	• Be sensitive. • Do not discourage other actions, unless they are harmful.
Unhappy with adverse effects	• Discuss possible adverse effects with patient in advance. • Teach the patient how to recognize and report adverse effects. • Assure patient that you are monitoring for adverse effects as well. • Consult the TB services regarding adverse effects and treat minor adverse effects as agreed with district TB specialist.
Lack of hope for recovery and reintegration into the community	• Emphasize that since TB is curable with proper treatment, patient can resume previous activities once treatment is complete. • Keep patient informed on progress of treatment.
Lack of skills for adherence (e.g., elderly patients with limited dexterity, or patients with mental illness)	• Come up with solutions, such as arranging someone to accompany patient to clinic.
Competing medical problems	• Discuss existing medical conditions with the patient. • Determine the most important actions necessary for treatment of the patient's multiple conditions. • Explain the importance of TB treatment. • Work with other care providers to identify solutions.
Lack of access to care	• Refer to social services, where available, for assistance with transportation, etc.
Language barrier	• Try to find an interpreter or family member who you can use to ensure that your message is being understood.
Preoccupied with other problems (e.g., fear of job loss)	• Reiterate importance of completing regimen • Emphasize ability to resume previous activities when treatment is complete. • Offer patient assistance in providing employer with proof of treatment completion and cure.
Poor relationship with health care system or workers	• Use communication skills to try to change these relationships.

A PHC provider must do everything possible to give every TB patient the best chance of treatment. By showing genuine concern and gentle persistence, the PHC provider can often persuade a patient to continue anti-TB treatment.

PHC providers involved in the continuation phase of therapy should:

- **Make appointments** when it is convenient for the patient; this may improve adherence.
- **Use incentives**, such as food or transportation assistance where available to encourage adherence. These may be especially effective for patients from socially vulnerable populations.
- **Enlist the support** of patient's family, if possible.
- **Refer patients** to specialized programmes such as assistance or counselling, to address the problems of a patient, including mental health and alcohol or substance abuse, if available.
- **Follow-up** this referral by asking the patient about these services during following visits.
- **Cooperate** with social workers or nurses where available to try to locate patients who are non-adherent, such as released prisoners and others.

Patients Who Default From Treatment

In some cases, despite the best efforts of the medical staff involved with directly observed treatment, patients will default. If a TB patient defaults on treatment or misses doses of anti-TB drugs, PHC providers should take the following actions as soon as possible:

- **Inform** the community or TB nurse (if such nurses are available);
- **Contact** the patient by phone or/and visit at home or in the workplace to check the reason for non-adherence, discuss the situation and encourage the patient to continue his treatment without interruptions;
- **Take** the daily dosage of the patient's anti-TB drugs with you, to provide directly observed treatment during your visit;
- **Determine** if other circumstances (such as other illness or family situations) are preventing the patient from reporting for treatment and work to resolve these circumstances;
- **Talk** to the patient's family and request that they provide assistance and encouragement to the patient;
- **Reiterate** importance of completing treatment to both the patient and family members; and
- **Report** immediately to the appropriate representative from the specialized TB services (in many cases, this is the district TB specialist), if the patient cannot be located.

Many TB patients come from socially vulnerable populations, including alcoholics, homeless people, migrants or ex-prisoners. For many patients in this group, their TB diagnosis is simply not the most important problem they are facing. These cases need close supervision. Many of the techniques suggested will be useful in working with these populations. Education and support, as well as addressing other concerns, may help motivate patients to care more about their health and thus be adherent. While education and support may seem less significant than TB treatment, they present one of the most important elements in the larger TB control effort.

Since TB can be spread to others and inadequately treated TB can develop drug resistance, some countries have passed regulations to force patients to take treatment, if no other methods have worked. If all other treatment attempts have failed and such national laws exist, then the appropriate enforcement authorities should be contacted.

9. Summary

PHC providers, facilitating overall promotion of health, play a crucial role in national and global TB control. Through accurate, timely detection and referral for treatment according to standardized treatment regimens, PHC physicians and other PHC providers can reduce morbidity and disease transmission and prevent the development of drug-resistant TB. By using the WHO recommended TB control strategy, the PHC provider assists in both supplying the patient with all the necessary requirements for cure and in reducing the burden of TB in the WHO European Region and the world.

TUBERCULOSIS

Annex I-A

Request for Sputum Microscopy Examination (TB 05)

1) Date _____
2) Name and address of the treatment unit _____
3) Patient's full name _____
4) Address (in full) _____

_____

5) Raion _____ 6) Date of birth _____ **7**) Sex: M ❐ F ❐
8) Reason for examination:
   ❐ Diagnosis ❐ Treatment monitoring follow-up, month _____ ❐ Other
9) Specimen identification numbers*: 1. _____ 2. _____ 3. _____
10) Patient's registration number** _____
11) Specimen collection dates: 1. _____ 2. _____ 3. _____
12) Signature of medical worker who collected sputum:

_____

*Three sputum samples should be collected for diagnosis purposes. Two sputum samples should be collected for treatment monitoring follow-up purposes.

**Enter the patient's TB registration number for registered patients on treatment.

Results of Smear Microscopy Examination (for laboratory use)

Lab serial number: _____

Sputum collection date	Specimen	Appearance of the specimen*			Result (Neg/ Pos)	Positive (grading)			
		M-P	Bl	S		Scanty	1+	2+	3+
	1					___AFB**			
	2					___AFB**			
	3					___AFB**			

*Visual appearance of the specimen: M-P – muco-purulent, Bl – blood-stained, S – saliva (If saliva, do not process).

**Indicate number of AFB per high-power field, if there are between 1 and 10 AFB present.

Date results reported: _____

Signature of lab technician: _____

[1] Annex 1 includes WHO accepted medical forms, which may be edited by national TB control programmes of individual countries in accordance with the specifics of national TB care delivery systems.

Annex I-B

TB01 Patient Treatment Card

Registration number (from TB 03)_____ Year _____ Quarter _____

Site of registration: _____

TB Patient Treatment Card (TB 01)

1. Name
2. Address and tel.: _____
3. Name, address and tel. of the next of kin:

_____

4. Sex: M ☐ F ☐
5. Date of birth: _____ 6. Age (_____)
7. Date of symptom onset: _____
8. Date when presented to physician with these symptoms: _____
9. Date when diagnosis was established: _____

1.1 Disease Classification

Pulmonary TB ☐	Extrapulmonary TB ☐ Organ(s)_____
Clinical form of pulmonary TB _____	Tuberculous pleuritis, upper respiratory TB or intrathoracic lymph node TB ☐

1.2 Patient Type

NEW ☐	TREATMENT AFTER FAILURE ☐
	TREATMENT AFTER DEFAULT ☐
	TRANSFERRED IN ☐
RELAPSE ☐	OTHERS ☐

1.4 Categories and standard treatment regimens in the intensive phase

Category 1	Category 2	Category 3
2HRZE(S) ☐	2 HRZES + 1 HRZE ☐	2 HRZE ☐

1.5 Intensive phase. Treatment regimen and TB drug dosage*
(indicate the daily dose in g)

Prescription Date	H	R	Z	E	S					

* Drugs: Isoniazid (H); Rifampicin (R); Pyrazinamide (Z); Streptomycin (S); Ethambutol (E)

1.3 Examination results

Month/treatment phase	Results of sputum examinations: Lab #	Test date	Smear	Culture	Drug sensitivity (S/R): H	R	S	E	X-ray (lung cavitation): Date	Result (+/-)	Weight (kg)
0*/GMS											
0**/TB Service											
2/3/ intensive phase											
3/4/ intensive phase extension											
5/ continuation phase											
At the end of treatment											

1.6 Intake of daily doses

Month \ Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Number of doses taken

Instructions for recording drug intake: Observed drug intake: nurse's initials; Non-observed drug intake: X – X; Drugs not taken: leave the cell empty

Number of daily doses taken in the intensive phase: _____

TB01 Patient Treatment Card (continued)

1.7 Categories and standard treatment regimens in the continuation phase

Category 1	Category 2	Category 3
4 HR or 4 H_3R_3 or 6 HE ☐ ☐ ☐	5 HRE ☐ or 5 H3R3E3 ☐	4 HR or 4H_3R_3 or 6 HE ☐ ☐ ☐

1.8 Continuation phase. Treatment regimen and TB drug dosage
(indicate the daily drug dose in g).

Prescription Date	H	R	E				

1.9 Intake of daily doses

Day / Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	Number of doses taken

Instruction for recording drug intake: **Observed drug intake:** nurse's initials; **Non-observed drug intake:** X – X; **Drugs not taken:** leave the cell empty | Number of daily doses taken in the continuation phase: _____

1.10 Treatment outcome

	Date
CURED (CONFIRMED BY SMEAR)	
CURED (CONFIRMED BY CULTURE)	
TREATMENT COMPLETED	
FAILURE (CONFIRMED BY SMEAR)	
FAILURE (CONFIRMED BY CULTURE)	
DEFAULTED	
TRANSFERRED OUT	
DIED	

1.11 Comments

_____
_____
_____
_____
_____

Annex 2: Additional Information[1]

The material in Annex 2 is primarily presented for informational purposes. Since diagnosis, classification of TB case, treatment and determining outcomes are all responsibilities of the specialized TB services, this information is not for active use by PHC providers, but rather for reference and general knowledge.

Annex 2-A

Classification of TB Cases

By Localisation and Bacteriology	
Pulmonary TB, smear-positive	• A patient with two or more initial sputum smear examinations positive for AFB; *or* • A patient with one sputum smear examination positive for AFB plus radiographic abnormalities consistent with active pulmonary TB as determined by a clinician; *or* • A patient with at least one sputum smear positive for AFB plus sputum culture positive for *M. tuberculosis.*
Pulmonary TB, Smear-Negative	• A patient with pulmonary TB who does not meet the above criteria for smear-positive TB. *Note:* Diagnostic criteria should include at least three sputum specimens negative for AFB, *and* radiographic abnormalities consistent with active pulmonary TB *and* no response to a course of broad-spectrum antibiotic *and* decision by a clinician to treat with a full course of anti-TB chemotherapy; *OR* A patient with at least three sputum smears negative for AFB but with sputum culture positive for *M. tuberculosis*
Extra-pulmonary TB	• A patient with TB of organs other than the lungs (e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and meninges). Diagnosis is based on one culture-positive specimen, or histological or strong clinical evidence consistent with active extrapulmonary TB, followed by a decision by a clinician to treat with a full course of anti-TB chemotherapy. • A patient diagnosed with both pulmonary and extra-pulmonary TB is classified as a case of pulmonary TB.

[1] The following are the accepted definitions used by WHO. These may be edited by national TB control programmes of individual countries in accordance with the specifics of national TB care delivery systems. The general meaning of the definitions should remain the same.

Classification of TB Cases (continued)

By Category of Registration on Diagnosis	
New	A patient who has never had treatment for TB or A patient who took anti-TB drugs for less than 1 month.
Relapse	A patient previously treated for TB who has been declared cured or treatment completed and is diagnosed with bacteriologically positive (smear or culture) TB.
Treatment After Failure	A patient who is started on a re-treatment regimen after having failed previous treatment.
Treatment After Default	A patient who returns to treatment with positive bacteriology, following interruption of treatment for 2 months or more.
Transfer In	A patient who has been transferred from another TB register to continue treatment.
Other	All other patients who do not fit the above definitions. This group includes chronic cases: a patient who is sputum smear-positive at the end of a re-treatment regimen. *Note:* Although smear-negative pulmonary and extrapulmonary cases may also be relapses, failures or chronic cases, this should be a rare event, supported by pathologic or bacteriologic evidence (culture).

Annex 2-B

Formulation and Dosages of Essential Anti-TB Drugs (Prescribed by TB Specialist)

Drug	Mode of Action	Dose Form	Strength	Recommended Dosage (dose range) in mg/kg	
				Daily	3 Times Weekly
Isoniazid (H)	Bactericidal	Tablet	100 mg, 300 mg	5 (4–6)	10 (8–12)
Rifampicin (R)	Bactericidal	Tablet or capsule	150 mg, 300 mg	10 (8–12)	10 (8–12)
Pyrazinamide (Z)	Bactericidal	Tablet	500 mg	25 (20–30)	35 (30–40)
Ethambutol (E)	Bacterio-static	Tablet	100 mg, 400 mg	15 (15–20)	30 (20–35)
Streptomycin (S)	Bactericidal	Powder for injection in vial	1 g	15 (12–18)	15 (12–18)

Annex 2-C

Recommended Treatment Regimen for Each Diagnostic Category (Prescribed by TB specialist)

TB Diagnostic Category	TB Patients	Treatment: Intensive Phase (Daily or 3 Times Weekly)[1]	Regimens: Continuation Phase (Daily or 3 Times Weekly)[1]
I	• New smear-positive patients • New smear-negative pulmonary TB with extensive parenchymal involvement • Severe concomitant HIV disease or severe forms of extra-pulmonary TB	2 HRZE[2]	4 HR or 6 HE daily[3]
II	Previously treated sputum smear-positive pulmonary TB (treated for at least one month): • Relapse • Treatment after interruption • Treatment failure[4]	2 HRZES/1 HRSE	5 HRE
III	• New smear-negative pulmonary TB (other than in Category I) • Less severe forms of extra-pulmonary TB	2 HRZE[5]	4 HR or 6 HE daily[3]
IV	• Chronic and MDR-TB cases (still sputum-positive after supervised re-treatments)[6]	Specially designed standardized or individualized regimens are suggested for this category	Specially designed standardized or individualized regimens are suggested for this category

H = Isoniazid R = Rifampicin Z = Pyrazinamide E = Ethambutol S = Streptomycin

[1] Direct observation of drug intake is required during the intensive phase of treatment in smear-positive cases and always in treatments involving rifampicin.
[2] Streptomycin may be used instead of ethambutol. In TB meningitis, ethambutol should be replaced by streptomycin.
[3] This regimen may be associated with a higher rate of treatment failure and relapse compared to the six-month regimen with rifampicin in the continuation phase.
[4] Whenever possible, drug sensitivity testing is recommended before prescribing Category II treatment in failure cases. It is recommended that patients with proven MDR-TB use Category IV regimens, which will only be administered in specialized facilities.
[5] Ethambutol may be omitted during the intensive phase of treatment for patients with non-cavitary, smear-negative pulmonary TB who are known to be HIV-negative, patients known to be infected with fully drug-susceptible bacilli and young children with primary TB.
[6] Contacts of patients with culture-proven MDR-TB should be considered for early culture and sensitivity testing.

Annex 2-D

Treatment Outcome Definitions for Sputum Smear-Positive TB Patients

Cured (Confirmed by smear and/ or culture)	A patient who is sputum smear-negative in the last month of treatment and on at least one previous occasion. OR A patient with culture-confirmed diagnosis of TB, who has completed one course of treatment and has negative culture results upon completion of the treatment.
Treatment Completed	A patient who has completed the treatment but who does not meet the criteria to be classified as cured or failure.
Died	A patient who died for any reason during the course of treatment.
Treatment Failure (Confirmed by smear and/ or culture)	A patient who is sputum smear-positive at 5 months or later during treatment. OR A patient who was sputum smear-negative, but sputum culture-positive in the beginning of treatment and remains culture-positive, when the treatment is complete. Also a patient who was sputum smear-negative before starting treatment and became smear-positive after completing the intensive phase of treatment.
Defaulted	A patient whose treatment was interrupted for two consecutive months or more.
Transferred Out	A patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known.
Treatment Success	The sum of patients cured and those who completed treatment.

Recommended Reading

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