

National Guidelines

for the Management of
Tuberculosis in Pakistan



Revised
Edition
2015



National TB Control Program

National Tuberculosis Control Program
Ministry Of National Health Services, Regulations & Coordination
Government of Pakistan
www.ntp.gov.pk



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FOREWORD

It is a matter of great pleasure and satisfaction that National TB Control Program has produced “Revised Edition” of National Guidelines for TB case Management”.

Pakistan currently harbors fifth highest burden of Tuberculosis alongside the fourth highest burden of Drug Resistant TB globally. In an estimated population of around 180 million with annual incidence of TB being 270/100,000, Pakistan produces about 510,000-730,000 new cases annually. As we move in the era of Sustainable Development Goals (SDGs), TB Control maintains a very high priority within the health sector.

National TB Control Program, working under the Ministry of Health Services, Regulation and Coordination, Government of Pakistan, in collaboration with all Provincial/Regional TB Control Programs, endorses and implements WHO recommended The End TB Strategy for effective control of this menace. The program entails free of cost diagnosis and treatment of registered TB patients through uninterrupted provision of quality assured anti TB drugs in the country.

This document on National Guidelines for TB Case Management has been developed in line with current WHO recommended TB control strategies for country wide implementation for effective TB care and control services in Pakistan.

I am sure that training on the National Guideline will enable the healthcare providers to benefit from current WHO recommended strategies and to deliver quality TB care to reduce the burden of disease. I appreciate the efforts made by all, involved in the development of this document. I wish all success to NTP in achieving the goal of effective Tuberculosis Control in Pakistan.

Dr. Ejaz Qadeer

National Manager

TB Control Program, Islamabad

EXECUTIVE SUMMARY

The purpose of these guidelines is to familiarize the readers with TB control Program components and standardized protocols for diagnosing and successfully treating sensitive and drug resistant tuberculosis patients. The guidelines are intended to be a reference document for all those who are involved in TB control activities in Pakistan.

Prompt, accurate diagnosis and effective treatment are not only essential for good patient care but also key elements in the public health response to tuberculosis and are the cornerstone of tuberculosis control. Thus, all providers who undertake evaluation and treatment of patients with tuberculosis must recognize that, not only are they delivering care to an individual, they are performing an important public health function that entails a high level of responsibility and individual patient and community is the main stakeholder.

These National Guidelines have incorporated the most up-dated WHO definitions and diagnostic treatment protocols and also other literature related to TB control in programmatic context to address sensitive and drug resistant TB in country situation and setting. It has been prepared in line with 'International Standards' for Tuberculosis Care'. These 'Standards' intended to facilitate the effective engagement of all care providers in delivering high-quality care for patients of all ages, including those with sputum smear-positive, sputum smear-negative, and extra pulmonary tuberculosis, tuberculosis caused by drug-resistant mycobacterium tuberculosis complex (M. tuberculosis) organisms, and tuberculosis combined with human immunodeficiency virus (HIV) infection.

This volume of National Guidelines has been organized to address all the essential TB control Program components. The guideline provides a most up-date information of TB epidemiology in Pakistan and strategies to control the disease in coming years. In addition to new definitions and concepts of TB control (passive and active), the guidelines also include the most up-date nationally recommendation on TB treatment regimen for adults and children and for DR-TB case. The new sections and chapters included in the guideline provide information on TB control Program management, capacity building, infection control, monitoring and evaluation.

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LIST OF ACRONYMS

ADR	Adverse Drug Reaction
AFB	Acid Fast Bacilli
ART	Anti-Retroviral Treatment
ATT	Anti Tuberculosis Treatment
B+	Bacteriologically Positive
BHU	Basic Health Unit
BMU	Basic Management Unit
CHTB	Child hood TB
CHW	Community Health Worker
CPT	Co-trimoxazole Preventive Therapy
DHO	District Health Officer
DHQ	District Headquarter Hospital
DLS	District Laboratory Supervisor
DMU	Drug Management Unit
DO	Direct Observation
DOTS	Directly Observed Treatment (short course)
DR TB	Drug Resistant TB
DRS	Drug Resistance Survey
DST	Drug Sensitivity Testing
DTC	District TB Coordinator
EDO	Executive District Officer
EPTB	Extra Pulmonary TB
EQA	External Quality Assurance
FLD	First Line Drug
FM	Fluorescent Microscopy

GDF	Global Drug Facility
GF	Global Fund
GNP	Gross National Product
GP	General Practitioner
HCP	Health Care Practitioner
HH Contacts	House Hold Contacts
HIV	Human Immunodeficiency Syndrome
HMIS	Health Management Information System
HPF	High-Power Field
HSS	Health System Strengthening
HTC	HIV testing counselling
IDPs	Internally Displaced Persons
IEC	Information, Education and Communication
IGRAs	Interferon Gamma Release Assays
INH	Isoniazid
IPT	INH Prophylaxis Therapy
LED	Light-emitting Diode Microscope
LED	Light Emitting Diode
LHW	Lady Health Worker
LPA	Line Probe Assay
LTBI	Latent TB Infection
M&E	Monitoring and Evaluation
MDG	Millennium Development Goals
MDR-TB	Multi-drug Resistant Tuberculosis
MO	Medical Officer
NGOs	Non-government Organizations

NSP	National Strategic Plan
NTP	National Tuberculosis Control Program
PCS	Pakistan Chest Society
PDL	Prison DOTS linkages
PHC	Primary Health Care
PHPM	Pharmaceutical Health Product Management
PITC	Provider Initiated Testing & Counselling
PLHIV	People Living with HIV
PMA	Pakistan Medical Association
PMDT	Programmatic Management of Drug Resistant TB
PPP	Public Private Mix
PRL	Provincial Reference Laboratory
PSCM	Procurement and Supply Chain Management
PTB	Pulmonary TB
PTCs	Presumptive of TB Cases
PTP	Provincial Tuberculosis Control Program
RDTs	Rapid Diagnostic Tests
RHC	Rural Health Centre
RR-TB	Rifampicin-resistant TB
SLD	Second Line Drug
TB	Tuberculosis
TBC	Tuberculosis Clinic
TBIC	Tuberculosis Infection Control
TCHs	Tertiary Care Hospitals
THQ	Tehsil Headquarter Hospital
TST	Tuberculin Skin Testing

WHO	World Health Organization
WRD	WHO-approved Rapid Diagnostics
XDR-TB	Extensively Drug-resistant TB

ANTI-TUBERCULOSIS DRUG ABBREVIATIONS

Am	Amikacin
Amx/Clv	Amoxicillin/Clavulanate
Cfx	Ciprofloxacin
Cfz	Clofazimine
Clr	Clarithromycin
Cm	Capreomycin
Cs	Cycloserine
E	Ethambutol
Eto	Ethionamide
Gfx	Gatifloxacin
H	Isoniazid
Km	Kanamycin
Lfx	Levofloxacin
Lzd	Linezolid
Mfx	Moxifloxacin
Ofx	Ofloxacin
PAS	P-aminosalicylic acid
Pto	Protionamide
R	Rifampicin
S	Streptomycin
Th	Thioacetazone
Trd	Terizidone
Vi	Viomycin
Z	Pyrazinamide

SECTION-I

TUBERCULOSIS CONTROL IN PAKISTAN

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CHAPTER 1

INTRODUCTION

1.1. COUNTRY OVERVIEW

Pakistan became a sovereign state in 1947. It spreads over 852,392 sq.kms and is home to 185 million people, making it the sixth most populous country in the world^[1]. Approximately 35% of the population is less than 15 years of age and about 60% of the total population lives in rural areas. Pakistan includes five provinces- Punjab (56% of the total population) is, population-wise, the largest province, followed by Sindh (23%), Khyber Pakhtunkhwa (17%), Balochistan (5%) and Gilgit-Baltistan (<1%); and three areas/regions- Azad Jammu Kashmir (AJK), Federally Administered Tribal Areas (FATA) and Islamabad Capital Territory (ICT).

Pakistan is one of the least developed countries in Asia with an estimated gross domestic product (GDP) per capita US\$1,339 in 2012-13. Natural disasters (floods and earthquakes) on-going war-on-terror, electricity and gas shortage have severely affected the country's economic growth and have consequences on the health care system. This in turn means that limited resources are available for important social sectors such as health and education. The annual health expenditure per capita is estimated at US \$ 39.4^[2]. Diseases of the poor, such as tuberculosis and other infectious diseases are major concerns in Pakistan as 26.2 % of deaths are attributable to communicable diseases^[3]. Unsafe drinking water, malnutrition, high population growth rate, low vaccine coverage, poverty and high illiteracy rate are conditions, which are co-prevalent with communicable diseases in the country.

1.2. EPIDEMIOLOGY OF TUBERCULOSIS IN PAKISTAN

TB Incidence and Prevalence: Tuberculosis (TB) is a major public health problem in Pakistan. As per WHO Global TB Report 2015 Pakistan ranks 5th amongst high burden countries for TB in the world^[4]. Estimated TB prevalence (all forms and all ages) is 341 cases per 100,000 populations which implies that between 510,000 - 730,000 individuals have active TB in the country at any given time. Based on this prevalence, the incidence was estimated at 270 TB cases per 100,000 populations.

TB Case Notification: The NTP Pakistan notified 298,446 TB cases (all forms) in 2013 which is 58% of case detected in the country. Among the total cases reported in 2013, 111,682 were new bacteriologically confirmed cases, 118,279 were sputum smear negative cases whereas 52,646 were extra-pulmonary cases. The ratio of pulmonary to extra-pulmonary cases among new TB patients has declined slightly in the last four years^[5]. In last few years, stagnant case notification has been observed in Pakistan which is an area of concern for NTP and the Program is addressing this by bringing in new initiatives in country.

Age and Gender Distribution: The NTP data show that TB is affecting mainly young adults and productive age groups. Among notified smear-positive TB cases 65% are aged less than 45 years, nearly 80% less than 55 years and 75% between 15 and 55 years. In 2013, among the total cases notified about 10% were children less than 15 years of age^[6]. The male to female rate ratio among notified TB cases in Pakistan is close to 1.

Geographic Distribution: The notification rate varies across provinces and regions: in 2013, the highest notified rate (all forms of TB) was in Punjab (189 per 100,000 populations) and the lowest in Balochistan (79 per 100,000 population)[8]. Among the national case notification, about 60% of TB cases were notified in Punjab, 20% in Sindh and 13% in the province of Khyber Pakhtunkhwa.

TB Mortality: The mortality rate of TB is declining every year in Pakistan and has reached 27 down from 69 deaths per 100,000 populations in 2013.

TB in special conditions and settings: Very few data on the social determinants and risk factor of TB is available in Pakistan. Data from a few pilot initiatives in correctional settings of the penitentiary system of Punjab suggest that the prevalence of TB in prisons is 1.3%. The NTP's existing sentinel surveillance system has indicated that the prevalence of HIV infection among TB patients was 0.4 percent in 2013.

Multi-Drug Resistant TB: According to the national DR survey (2012-13), the DR-TB incidence has been estimated at 3.7% among notified new pulmonary cases and 18.1% among retreatment patients. In 2014, 32% of the total incident drug resistant TB patients were detected and enrolled on second line treatment.

CHAPTER 2

TUBERCULOSIS CONTROL IN PAKISTAN

2.1. COMMITMENT TO TUBERCULOSIS CONTROL

The Health Policy of Pakistan formulated in the year 2001 makes a direct reference for controlling TB in Pakistan using the WHO-recommended strategy of Directly Observed Treatment Short Course (DOTS). Tuberculosis was subsequently declared a national emergency by the Ministry of Health on March 24, 2001 and all partners were requested to join hands with the government in an Islamabad declaration adopted on the same day. The federal government along with its provincial counter-parts is committed to fight TB and has allocated substantial public sector funds to control TB in the country. Similarly many donors such as Global Fund, KFW, and WHO have contributed significantly by providing financial and technical assistance to the TB control Program in Pakistan.

The Tuberculosis Control Program and Health Sector Devolution: Since the inception of the TB control Program, its activities have been integrated in Primary Health Care (PHC) at grass root level. The districts are the implementation units and are responsible for the care delivery processes including Program planning, training of care providers, case detection, case management, monitoring and supervision whereas the Provincial Tuberculosis Control Programs (PTPs) provides the districts an overall technical and material support (drugs, lab supplies, hard ware etc.) to carry out their functions. The National TB Control Program (NTP) being the custodian of the Program is responsible for policy guidelines, technical support, coordination, monitoring and evaluation, research and financial resource generation by coordinating with national and international donor and technical agencies.

2.2. GLOBAL TB STRATEGY AND NTP PAKISTAN

The TB control globally and in Pakistan has been evolved in various stages. The current status is as following:

Global TB targets and MDGs

2015: 50% reduction in TB prevalence and death rates by 2015

2050: TB will be eliminated as a global public health problem (global incidence<1 per million

2015: Goal 6: Combat HIV/AIDS, malaria and other diseases

Target 8:

Indicator 6.9: To have halted by 2015 and begun to reverse the incidence, prevalence and deaths associated with TB

Indicator 6.10: Proportion of TB cases detected and cured under DOTS (70/85)

Sustainable Development Goals (SDGs)

Unlike the current MDGs, which tried to extrapolate global trends to arrive at global targets, countries should instead be asked to come up with their own targets, preferably above a universally agreed minimum level, in a one-world approach. Each country, based on its own context and patterns, should set its own targets. Global targets could then be deduced by looking at the weighted average of country targets as well as global trends.

SDG- Goal 4: Good Health for the Best Possible Physical, Mental and Social Well-being

Post 2015 Global TB Strategy - Three Pillars

Pillar-I: Innovative TB Care

Pillar-II: Bold Policies and Supportive System

Pillar-III: Intensified Research and Innovation

Goals and Targets- Beyond 2015

Vision: A world free of tuberculosis – Zero deaths, disease and suffering due to tuberculosis

Goal: End the global tuberculosis epidemic

Milestones for 2025: a) 75% reduction in tuberculosis deaths (compared with 2015); b) 50% reduction in tuberculosis incident rate (compared with 2015, less than 55 TB cases per 100,000 population); and c) No affected families facing catastrophic costs due to tuberculosis.

Targets for 2035: a) 95% reduction in TB deaths (compared with 2015); b) 90% reduction in tuberculosis incidence rate (compared with 2015, less than 10 TB cases per 100,000 population); and c) No. affected families facing catastrophic costs due to TB.

Principles: a) Government stewardship and accountability, with monitoring and evaluation; b) Strong coalition with civil society organizations and communities; c) Protection and promotion of human rights, ethics and equality; and d) Adaptation of the strategy and targets at country level, with global collaboration.

NTP Pakistan's Response – National TB Control Strategic Plan “Vision 2020”

The National TB Strategic Plan “Vision 2020” entails developing innovative strategies that will:

- 1- Improve the performance and impact of TB control by maximizing public sector investment and accountability in TB control activities.
- 2- Address sensitive and drug resistant TB by: (a) reducing diagnostic delays, (b) reducing the duration and improving the efficacy of treatment, (c) preventing disease, and (d) increasing access to DOTS and DR-TB treatment, etc.
- 3- Invest in new diagnostic and TB management tools and approaches that are less labor intensive, more cost-effective, and can be delivered close to patients to minimize the health

workforce burden and help improve patient access, thereby increasing case detection and enhance treatment success rates.

- 4- Universal access to TB services, which implies expanding TB DOTS through all types of healthcare providers including the large and currently unregulated private sector
- 5- Prioritize research that has the potential to change policy and practice in TB care in the country.

The NSP vision 2020 entails achieving the following:

Vision: TB Free Pakistan

Mission: To ensure universal access to quality diagnosis and treatment for people with TB.

Goal: To reduce 50%, the prevalence of TB by 2025 in comparison to 2012.

Objectives ^[7]:

- i) To increase the contribution of public sector TB control Program funding at least 3 times by 2016 onwards in comparison to 2013;
- ii) To increase the number of notified TB cases from 298,981 in 2013 to at least 420,000 by 2020 while maintaining the treatment success rate at least at 93%
- iii) To reduce, by at least 5% per year from 2018 onwards, the prevalence of MDR-TB among TB patients who have never received any TB treatment;
- iv) To optimize and sustain the programmatic deliverables (technical and managerial) at operational level by 2018

2.3. TB CONTROL PROGRAM MANAGEMENT IN PAKISTAN

National TB Control Program was revived in year 2000 with the mandate to design and regulate TB control activities in the country with indigenous resources and donor support and since then TB control Program interventions are implemented by the districts through an integrated approach in primary, secondary and tertiary health care facilities.

The TB Program management roles at district, provincial and federal levels have been redefined after devolution and they are as under;

Districts Health system:

- Implementation of TB control interventions through public and private sector
- Coordination with other departments for effective management of Tuberculosis
- Service delivery through Basic Management unit (Rural Health Center/ Basic Health unit)

Provincial TB Control Program:

- Development of province specific strategic plan and planning documents (PC-1)
- Oversight implementation of TB control interventions
- Technical assistance to districts
- Coordination with implementing & bilateral partners
- Logistic support to districts
- Data validation
- Monitoring & supervision

National TB Control Program:

- Coordination and Technical assistance to provinces and districts
- Development of national strategic plan and planning documents (PC-1)
- Policy formulation
- Resource generation especially foreign support
- Disease surveillance
- International representation

2.4. INTERNATIONAL STANDARDS FOR TUBERCULOSIS CARE: DIAGNOSIS, TREATMENT AND PUBLIC HEALTH

The NTP Pakistan is following the international standards for TB care to improve the quality of Program implementation.

The standards are as follows ^[8]:

STANDARDS FOR DIAGNOSIS

Standard 1. To ensure early diagnosis, providers must be aware of individual and group risk factors for tuberculosis and perform prompt clinical evaluations and appropriate diagnostic testing for persons with symptoms and findings consistent with tuberculosis.

Standard 2. All patients, including children, with unexplained cough lasting two or more weeks or with unexplained findings suggestive of tuberculosis on chest radiographs should be evaluated for tuberculosis.

Standard 3. All patients, including children, who are suspected of having pulmonary tuberculosis and are capable of producing sputum should have at least two sputum specimens submitted for smear microscopy or a single sputum specimen for X-pert® MTB/Rif¹ testing in a quality-assured laboratory.

Patients at risk for drug resistance, who have HIV risks, or who are seriously ill, should have X-pert MTB/Rif performed as the initial diagnostic test. Blood-based serologic tests and interferon-gamma release assays should not be used for diagnosis of active tuberculosis.

Standard 4. For all patients, including children, suspected of having extra pulmonary tuberculosis, appropriate specimens from the suspected sites of involvement should be obtained for microbiological and histological examination.

An X-pert MTB/Rif test is recommended as the preferred initial microbiological test for suspected tuberculous meningitis because of the need for a rapid diagnosis.

Standard 5. In patients suspected of having pulmonary tuberculosis whose sputum smears are negative, X-pert MTB/Rif and/or sputum cultures should be performed. Among smear- and X-pert MTB/Rif negative persons with clinical evidence strongly suggestive of tuberculosis, anti-tuberculosis treatment should be initiated after collection of specimens for culture examination.

Standard 6. For all children suspected of having intrathoracic (i.e., pulmonary, pleural, and mediastinal or hilar lymph node) tuberculosis, bacteriological confirmation should be sought through examination of respiratory secretions (expectorated sputum, induced sputum, gastric lavage) for smear microscopy, and X-pert MTB/Rif test, and/or culture.

STANDARDS FOR TREATMENT

Standard 7. To fulfill her/his public health responsibility, as well as responsibility to the individual patient, the provider must prescribe an appropriate treatment regimen, monitor adherence to the regimen, and, when necessary, address factors leading to interruption or discontinuation of treatment. Fulfilling these responsibilities will likely require coordination with local public health services and/or other agencies.

Standard 8. All patients who have not been treated previously and do not have other risk factors for drug resistance should receive a WHO-approved first-line treatment regimen using quality assured drugs. The initial phase should consist of two months of isoniazid, Rifampicin, pyrazinamide, and ethambutol. The continuation phase should consist of isoniazid and Rifampicin given for 4 months. The doses of anti-tuberculosis drugs used should conform to WHO recommendations. Fixed-dose combination drugs may provide a more convenient form of drug administration. Ethambutol may be omitted in children who are HIV-negative and who have non-cavitary tuberculosis.

¹ As of this writing, X-pert ® MTB/Rif (Cepheid Corp. Sunnyvale, California, USA) is the only rapid molecular test approved by WHO for initial use in diagnosing tuberculosis, thus, it is specifically referred to by its trade name throughout this document.

Standard 9. A patient-centered approach to treatment should be developed for all patients in order to promote adherence, improve quality of life, and relieve suffering. This approach should be based on the patient's needs and mutual respect between the patient and the provider.

Standard 10. Response to treatment in patients with pulmonary tuberculosis (including those with tuberculosis diagnosed by a rapid molecular test) should be monitored by follow up sputum smear microscopy at the time of completion of the initial phase of treatment (two months). If the sputum smear is positive at completion of the initial phase, sputum microscopy should be performed again at 3 months and, if positive, rapid molecular drug sensitivity testing (line probe assays or X-pert MTB/Rif) or culture with drug susceptibility testing should be performed. In patients with extra pulmonary tuberculosis and in children, the response to treatment is best assessed clinically.

Standard 11. An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms, and the community prevalence of drug resistance (if known), should be undertaken for all patients. Drug susceptibility testing should be performed at the start of therapy for all patients at a risk of drug resistance. Patients who remain sputum smear-positive at completion of 3 months of treatment, patients in whom treatment has failed, and patients who have been lost to follow up or relapsed following one or more courses of treatment should always be assessed for drug resistance. For patients in whom drug resistance is considered to be likely an X-pert MTB/Rif test should be the initial diagnostic test. If Rifampicin resistance is detected, culture and testing for susceptibility to isoniazid, fluoroquinolones, and second-line injectable drugs should be performed promptly. Patient counseling and education, as well as treatment with an empirical second-line regimen, should begin immediately to minimize the potential for transmission. Infection control measures appropriate to the setting should be applied.

Standard 12. Patients with or highly likely to have tuberculosis caused by drug-resistant (especially MDR/XDR) organisms should be treated with specialized regimens containing quality-assured second-line anti tuberculosis drugs. The doses of anti-tuberculosis drugs should conform to WHO recommendations. The regimen chosen may be standardized or based on presumed or confirmed drug susceptibility patterns. At least five drugs, pyrazinamide and four drugs to which the organisms are known or presumed to be susceptible, including an injectable agent, should be used in a 6–8 month intensive phase, and at least 3 drugs to which the organisms are known or presumed to be susceptible, should be used in the continuation phase.

Treatment should be given for at least 18–24 months beyond culture conversion. Patient-centered measures, including observation of treatment, are required to ensure adherence. Consultation with a specialist experienced in treatment of patients with MDR/XDR tuberculosis should be obtained.

Standard 13. An accessible, systematically maintained record of all medications given, bacteriologic response, outcomes, and adverse reactions should be maintained for all patients.

Standards for Addressing HIV Infection and other Co-Morbid Conditions

Standard 14. HIV testing and counseling should be conducted for all patients with, or suspected of having, tuberculosis unless there is a confirmed negative test within the previous two months. Because of the close relationship of tuberculosis and HIV infection, integrated approaches to prevention, diagnosis, and treatment of both tuberculosis and HIV infection are recommended in areas with high HIV prevalence. HIV testing is of special importance as part of routine management of all patients in areas with a high prevalence of HIV infection in the general population, in patients

with symptoms and/or signs of HIV-related conditions, and in patients having a history suggestive of high risk of HIV exposure.

Standard 15. In persons with HIV infection and tuberculosis who have profound immunosuppression (CD4 counts less than 50 cells/mm³), ART should be initiated within 2 weeks of beginning treatment for tuberculosis unless tuberculous meningitis is present. For all other patients with HIV and tuberculosis, regardless of CD4 counts, antiretroviral therapy should be initiated within 8 weeks of beginning treatment for tuberculosis. Patients with tuberculosis and HIV infection should also receive cotrimoxazole as prophylaxis for other infections.

Standard 16. Persons with HIV infection who, after careful evaluation, do not have active tuberculosis should be treated for presumed latent tuberculosis infection with isoniazid for at least 6 months.

Standard 17. All providers should conduct a thorough assessment for co-morbid conditions and other factors that could affect tuberculosis treatment response or outcome and identify additional services that would support an optimal outcome for each patient. These services should be incorporated into an individualized plan of care that includes assessment of and referrals for treatment of other illnesses. Particular attention should be paid to diseases or conditions known to affect treatment outcome, for example, diabetes mellitus, drug and alcohol abuse, under nutrition, and tobacco smoking. Referrals to other psychosocial support services or to such services as antenatal or well-baby care should also be provided.

STANDARDS FOR PUBLIC HEALTH AND PREVENTION

Standard 18. All providers should ensure that persons in close contact with patients who have infectious tuberculosis are evaluated and managed in line with international recommendations. The highest priority contacts for evaluation are:

- Persons with symptoms suggestive of tuberculosis
- Children aged <5 years
- Contacts with known or suspected immune compromised states, particularly HIV infection
- Contacts of patients with MDR/XDR tuberculosis

Standard 19. Children <5 years of age and persons of any age with HIV infection who are close contacts of a person with infectious tuberculosis, and who, after careful evaluation, do not have active tuberculosis, should be treated for presumed latent tuberculosis infection with isoniazid for at least six months.

Standard 20. Each health care facility caring for patients who have, or are suspected of having, infectious tuberculosis should develop and implement an appropriate tuberculosis infection control plan to minimize possible transmission of *M. tuberculosis* to patients and health care workers.

Standard 21. All providers must report both new and re-treatment tuberculosis cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies.

SECTION-II

TUBERCULOSIS CARE AND PREVENTION

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CHAPTER 3

UNDERSTANDING TUBERCULOSIS DISEASE

3.1. CAUSE OF THE DISEASE

Tuberculosis is an infectious, systemic, chronic granulomatous disease caused in the vast majority of cases by a bacterium called *Mycobacterium Tuberculosis* (tubercle bacilli). The organism was identified by Robert Koch on 24th March 1882. This day is now commemorated as WORLD TB day every year.

3.2. TRANSMISSION OF INFECTION

Tuberculosis is transmitted to other persons by infected droplet generated by coughing or sneezing of patient having pulmonary Tuberculosis. These tiny droplets dry rapidly, attach themselves to fine dust particles and the smallest of them may remain suspended in the air for several hours. Only those particles that are less than 10 micron in diameter reach the pulmonary alveoli of the healthy individual through inhalation resulting in infection.

3.3. HOW DOES TUBERCULOSIS DEVELOP?

Infection occurs almost exclusively by inhalation of tubercle bacilli. Tuberculosis spreads from the primary lung lesion to other parts of the body via the blood stream, lymphatic or by direct extension, and in this way may affect any organ in the body.

3.4. WHAT ARE SYMPTOMS OF TUBERCULOSIS?

Pulmonary Tuberculosis: The most common symptom of pulmonary TB is a productive cough for more than 2 weeks, which may be accompanied by other respiratory symptoms (shortness of breath, chest pain, haemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

Extra Pulmonary Tuberculosis: In case of Extra pulmonary TB, symptoms depend on the organs involved, for example:

- Swelling, occasionally with pus drainage when lymph nodes are affected;
- Pleural effusion (dry cough, shortness of breath, heaviness on the affected side)
- Pain and swelling when joints are involved;
- Headache, fever, stiffness of the neck and mental confusion in tuberculosis meningitis;
- Loss of function in lower limbs when there is gibbous and spinal involvement;
- Infertility when genital reproductive tract is affected

3.5. TB CASE DEFINITIONS

This section describes the revised definitions of sensitive TB cases and their classification^[9]. The definitions related to DR-TB and TB-HIV is described in related sections.

Presumptive TB refers to a patient who presents with symptoms or signs suggestive of TB (previously known as a *TB suspect*).

A.1 Case definitions

- A **bacteriologically confirmed TB case** is one from whom a biological specimen is positive by smear microscopy, culture or WHO Approved Rapid Diagnostic (WRD) such as X-pert MTB/Rif. All such cases should be notified, regardless of whether TB treatment has started.
- A **clinically diagnosed TB case** is one who does not fulfill the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extra pulmonary cases without laboratory confirmation.

Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

Bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to:

- anatomical site of disease
- history of previous treatment
- drug resistance
- HIV status.

A.1.1 Classification based on anatomical site of disease

Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra-pulmonary TB. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB.

Extra pulmonary tuberculosis (EPTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

A.1.2 Classification based on history of previous TB treatment (patient registration group)

Classifications based on history of previous TB treatment are slightly different from those previously published. They focus only on history of previous treatment and are independent of bacteriological confirmation or site of disease.

New patients have never been treated for TB or have taken anti-TB drugs for less than 1 month.

Previously treated patients have received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment as follows:

- **Relapse patients** have previously been treated for TB, were declared *cured* or *treatment completed* at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by re-infection).
- **Treatment after failure patients** are those who have previously been treated for TB and whose *treatment failed* at the end of their most recent course of treatment.
- **Treatment after loss to follow-up patients** have previously been treated for TB and were declared *lost to follow-up* at the end of their most recent course of treatment. (These were previously known as *treatment after default* patients.)
- **Other previously treated patients** are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.
- **Patients with unknown previous TB treatment history** do not fit into any of the categories listed above.

New and relapse cases of TB are **incident** TB cases.

CHAPTER 4

TUBERCULOSIS CASE FINDING AND DIAGNOSIS

Of the 9.0 million (range, 8.7–9.4 million) incident cases of TB estimated to have occurred. Only 5.7 million were both detected and notified to national TB Programs (NTP) or national surveillance systems, giving a case detection rate of 64% (range, 61–66%). This leaves a gap of approximately 3.3 million people with TB who were “missed”, either because they were not diagnosed or because they were diagnosed but not reported.

About 74% of the “missed cases” exist in 10 countries and Pakistan stands third among these countries and contribute 7% of the globally missed TB cases. This accounts for more than 200,000 TB cases missed annually in Pakistan against estimated 600,000 incident cases.

Major efforts to ensure that all detected cases are reported to NTPs and to improve access to care to reduce levels of under-diagnosis are needed. Top priority actions to reduce levels of underreporting include intensified collaboration with public hospitals and the private sector; mandatory notification of cases; and specific efforts to compile data on diagnosed cases from facilities that are not routinely reporting to national surveillance systems. In many districts, improving access to basic TB diagnostic and treatment services is essential to reduce levels of under-diagnosis.

4.1. TB CASE FINDING APPROACHES

To improve tuberculosis control, patient with active TB disease must be diagnosed quickly and treated immediately. Passive case finding approaches were used mostly for TB case finding in the past however now Program also recommends using active case finding approaches in certain population to enhance case finding. Main difference between two approaches is described below.

4.1.1. PASSIVE TUBERCULOSIS CASE FINDING

Relies on people seeking medical help because they feel unwell, Examination is recommended of:

- Presumptive TB cases (cough >two weeks or with relevant symptoms) who present themselves at health facilities
- Patient with radiological examination of the chest showing an abnormality consistent with Tuberculosis.

Passive case finding is likely to delay the diagnosis and treatment of tuberculosis and increases *M. tuberculosis* transmission

4.1.2. ACTIVE TUBERCULOSIS CASE FINDING

Where health workers seek out and diagnose individuals with TB mainly in the communities who have not sought care on their own initiative— The ultimate goal of active TB case finding is to reduce TB transmission in the community through improved case detection and reduction in diagnostic delays.

Active TB case finding aims to reduce barriers for early TB case detection, including delays in presentation to health facilities, identification of the person as a Presumptive TB case, and initiation of appropriate investigations.

The World Health Organization (WHO), which already recommends active tuberculosis case finding in HIV-infected individuals as part of its HIV/TB “Four I's” strategy

The Program recommends active case findings among

- Household contacts of all pulmonary TB patients
- Marginalized population e.g. Urban slums
- High vulnerable population prisons and institutes
- Internally displaced population

LHWs/volunteer's/community workers can be mobilized for TB case finding in community or special chest camps can be organized in community for active screening.

4.2. DIAGNOSTIC TOOLS FOR TUBERCULOSIS:

4.2.1. AFB SMEAR MICROSCOPY

Mycobacteria are distinguished from other micro-organisms by thick lipid-containing cell-walls that retain biochemical stains despite decolourisation by acid-containing reagents (so-called 'acid-fastness').

Microscopy of sputum smears is simple and inexpensive, quickly detecting infectious cases of pulmonary TB; Sputum specimens from patients with pulmonary TB - especially those with cavitory disease - often contain sufficiently large numbers of acid-fast bacilli to be readily detected by microscopy.

There is not sufficient evidence that processed (e.g. concentrated or chemically treated) sputum specimens provide superior results to direct smear microscopy. Implementation of such methods in programmatic settings is therefore not recommended.

Microscopy for acid-fast bacilli (AFB) cannot distinguish *Mycobacterium tuberculosis* from NTM, nor viable from non-viable organisms, or drug-susceptible from drug-resistant strains. However, Direct smear microscopy is relatively insensitive as at least 5,000 bacilli per millilitre of sputum are required for direct microscopy to be positive. Smear sensitivity is further reduced in patients with extra-pulmonary TB, those with HIV-co-infection, and those with disease due to non-tuberculous mycobacteria (NTM).

Conventional light microscopy: Ziehl-Neelsen (ZN) light microscopy performed directly on sputum specimens is suitable for all laboratory service levels, including peripheral laboratories at primary health care centres or districts hospitals. In general, one ZN microscopy centre per 100,000 populations is sufficient; however, expansion of ZN microscopy services should also take into

account the location and utilization of existing services, urban/rural population distribution, and specimen transport mechanisms.

Conventional fluorescent microscopy: Fluorescence microscopy is on average 10% more sensitive than ZN microscope. Conventional fluorescent microscopes require technical expertise and capital and running costs is considerably higher. Conventional fluorescent microscopy is therefore recommended at intermediate laboratory level where more than 100 smears are examined per day.

Light-emitting diode (LED) fluorescent microscopy: LED microscopes are cost effective as require less power, are able to run on batteries, the bulbs have a very long half-life. WHO evaluation (2007) confirmed the diagnostic accuracy of LED microscopy compared to conventional fluorescent microscopy, and superior efficiency of LED over conventional ZN microscopy. It is therefore recommended that conventional fluorescence microscopy be replaced by LED microscopy and that LED microscopy be phased in as an alternative for conventional ZN light microscopy in both high and low-volume laboratories.

4.2.2. X-PERT MTB/Rif ASSAY

The X-pert MTB/Rif is a **Rapid Molecular Test for diagnosis of TB** assay can detect both TB and resistance to Rifampicin in less than two hours (in a single test) and currently is the only fully automated cartridge based real-time DNA based test. It is more sensitive than microscopy and detect MTB even when present in very small numbers detection limit is 136(MTB/ML of sputum) and thus has a high sensitivity in smear-negative tuberculosis. Sensitivity of a single X-pert MTB/Rif test in smear-negative/culture-positive patients is reported to be 72.5% and increased to 90.2% when three samples are tested. X-pert MTB/Rif specificity is 99%.

Table 1: Reporting pattern and interpretation of results of X-pert MTB Rif

S.N	REPORT	DR-TB RISK ASSESSMENT	INTERPRETATION	ACTION
1	MTB Detected Rif resistance NOT detected	No previous history of ATT	Definite TB case NO Rifampicin resistance	Start Cat-I
		History of previous ATT	Definite TB case NO Rifampicin resistance	Start Cat- II
		History of Cat-II Failure	Definite TB case No Rifampicin resistance	Start Cat-II and transport sample/Refer patient for pheno DST
2	MTB Detected Rifampicin Resistance Detected	No previous history of ATT	Definite TB case with Rifampicin resistance	Repeat X-pert MTB/Rif assay – If -RR Not detected - start on FLD-Cat-I -RR detected –reg and start on SLD

		History of previous ATT	Definite TB case with Rifampicin resistance	Refer patient to MDR treatment site enroll patient on SLD and send specimen for FL and SLDST.
3	MTB NOT detected		MTB Not detected but not excluded	Culture / clinical evaluation diagnosis

The MTB/Rif assay is simple to perform with minimal training, is not prone to cross-contamination, and requires minimal bio-safety facilities (similar to smear microscopy)

WHO recommendation on use of X-pert MTB/Rif: WHO endorsed the use of X-pert MTB/Rif assay in 2010. Policy recommendations on the X-pert MTB/Rif assay® (X-pert MTB/Rif) were issued by WHO early in 2011 and updated in 2013

For the diagnosis of pulmonary TB and Rifampicin resistance

- X-pert MTB/Rif should be used as an initial diagnostic test in individuals (adults and children) presumptive case of DR or HIV-associated TB
- X-pert MTB/Rif may be used as an initial diagnostic test in individuals (adults and children) presumed to have TB (conditional recommendation based on resource implication)
- X-pert MTB/Rif may be used as a follow-on test to microscopy in adults presumed to have TB but not at risk of DR-TB or HIV associated TB (conditional recommendation based on resource implication)

For the diagnosis of extra-pulmonary TB and Rifampicin resistance

- X-pert MTB/Rif should be used in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid specimens from patients presumed to have TB meningitis
- X-pert MTB/Rif may be used as a replacement test for usual practice (including conventional microscopy, culture, and/or histopathology) for testing of specific non-respiratory specimens (lymph nodes and other tissues) from patients presumed to have extra pulmonary TB (conditional recommendation).

4.2.3. CULTURE AND SPECIES IDENTIFICATION

Mycobacterial culture and identification of *M. tuberculosis* provide a definitive diagnosis of TB and is the gold standard for diagnosis. It can detect far lower numbers of AFB, the detection limit being around 100 organisms per ml and thus can detect cases earlier (often before they become infectious). Culture also provides the necessary isolates for conventional DST. Moreover, culture makes it possible to identify the mycobacterial species. It therefore seems that, for the diagnosis of tuberculosis, both the sensitivity and the specificity of culture methods are better than those of smear microscopy as well as X-pert MTB/Rif assay. However, it is not considered for use as an initial

diagnostic test because it demands more resources, is technically complex and requires infrastructure of biosafety laboratory for processing and requires a much longer wait of 2-6 weeks for results (1-2 weeks on liquid culture media and 4-8 weeks on solid culture media) than both the X-pert MTB/Rif test and sputum-smear microscopy, both of which can provide final test results in less than 1 day.

Solid and liquid culture methods are suitable for Regional /Provincial and National reference laboratories (or regional laboratories in large countries). Usually, one culture laboratory is adequate to cover 500,000 - 1 million populations. Solid culture methods are less expensive than liquid culture systems, but results are invariably delayed due to the slow growth of mycobacteria. Liquid culture increases the case yield by 10% over solid media, and automated systems reduce the diagnostic delay to days rather than weeks. Liquid systems are, however, more prone to contamination and the manipulation of large volumes of infectious material mandates appropriate and adequate biosafety measures.

Use of culture is recommended in routine practice

- To obtain Culture isolates for conventional DST
- Treatment monitoring of drug resistant TB patient on second line drugs
- Smear and X-pert MTB/Rif negative presumptive TB case with difficulty in clinical diagnosis

4.2.4. LABORATORY TEST FOR DIAGNOSIS OF TB INFECTION

There are two kinds of tests that are used to determine if a person has been infected with TB bacteria: the tuberculin skin test and TB blood tests (see Interferon Gamma release assay).

TUBERCULIN TEST

TST requires two patient visits, results are available in 48-72hrs, TST is not expensive, requires an injection into the skin, adequately trained staff, and no special laboratory infrastructure or supplies. BCG vaccination may cause false-positive results in younger persons.

The tuberculin test is recommended in clinical work with children under 5 years of age, where a positive test is more likely to reflect recent infection with Tuberculosis and a much higher risk of developing disease. Other than in children, TST has a limited value in clinical work, in high prevalence countries like Pakistan. A "positive" tuberculin test is infrequently followed by disease and a "negative" tuberculin test does not exclude active tuberculosis

TUBERCULOSIS INTERFERON GAMMA RELEASE ASSAYS ^[10]:

Research over the past decade has resulted in the development of two commercial interferon gamma release assays (IGRAs), based on the principle that the T-cells of individuals who have acquired TB infection respond to re-stimulation with Mycobacterium tuberculosis-specific antigens by secreting interferon gamma (IFN- γ).

IGRAs were explicitly designed to replace the tuberculin skin test (TST) in diagnosis of LTBI, and were not intended for diagnosis of active TB. Because IGRAs (like the TST) cannot distinguish LTBI from active TB, these tests are expected to have poor specificity for active TB in high-burden settings due to a high background prevalence of LTBI.

In recent years, IGRAs have become widely endorsed in high-income countries for diagnosis of latent TB infection (LTBI) and several guidelines (albeit equivocal) on their use have been issued.

The WHO Stop TB Department (WHO-STB) commissioned systematic reviews on the use of IGRAs in low- and middle-income countries, in pre-defined target groups. And general conclusion drawn are 1) There is insufficient data and low quality evidence on the performance of IGRAs in low- and middle-income countries, typically those with a high TB and/or HIV burden; 2) IGRAs and the TST cannot accurately predict the risk of infected individuals developing active TB disease; 3) Neither IGRAs nor the TST should be used for the diagnosis of active TB disease; 4) IGRAs are costlier and technically complex to do than the TST. Given comparable performance but increased cost, replacing the TST by IGRAs as a public health intervention in resource-constrained settings is not recommended.

WHO recommendation on Use of IGRA:

IGRAS should not be used in low- and middle-income countries for:

- The diagnosis of pulmonary or extra-pulmonary TB, nor for the diagnostic work-up of adults (including HIV-positive individuals) presumptive case of active TB in these settings (strong recommendation).

IGRAS SHOULD NOT REPLACE THE TST IN LOW- AND MIDDLE-INCOME COUNTRIES for

- The diagnosis of latent TB infection in
 - In children, nor for the diagnostic work-up of children (including HIV positive children)
 - In individuals living with HIV infection
- The screening of latent TB infection in adult and paediatric contacts, or in outbreak investigation.

4.2.5. SEROLOGICAL TEST

Dozens of commercial serological tests for tuberculosis are being marketed in many parts of the world. An updated systematic review was commissioned by WHO to synthesize the evidence on the diagnostic accuracy of commercial serological tests for pulmonary and extra-pulmonary tuberculosis. Commercial serological tests provide inconsistent and imprecise findings resulting in highly variable values for sensitivity and specificity. There is no evidence that existing commercial serological assays improve patient-important outcomes, and high proportions of false-positive and false-negative results adversely impact patient safety. Overall data quality was graded as very low and **it is strongly recommended that these tests not be used for the diagnosis of pulmonary and extra-pulmonary TB** ^[11].

4.2.6. HISTOPATHOLOGY

Histological examination of biopsied tissue may support a diagnosis of tuberculosis (caseating granulomas) when bacteriology is negative or cannot be done, however histology is non-specific. The patient's risk of tuberculosis should be considered to avoid misclassifying non-caseating

granulomatous processes due to tuberculosis as sarcoidosis, Crohn's disease, or other granulomatous disease.

Always ensure enough tissue is available (collected in normal saline) for molecular assay or culture if TB is suspected.

4.2.7. OTHER LAB TEST

Blood examination e.g. Hb, CBC and ESR are not useful tests as anaemia is more likely to be due to other causes than TB, WBC is usually normal or lower than normal in TB and ESR is usually raised in TB but in other conditions too. A normal result however does not exclude active TB

4.3. ROLE OF X-RAYS IN DIAGNOSIS OF TUBERCULOSIS

The sputum smear examination for AFB should be performed in all PTB presumptive cases as initial diagnostic test. Radiological examination is recommended for diagnoses of TB in patients with i) two AFB smear negative microscopy results ii) children and iii) young adult who cannot produce sputum and iv) patients suffering from miliary or extra-pulmonary tuberculosis.

Chest X-ray plays an important role in the diagnosis of TB and non-TB chest diseases. However, the radiological diagnosis of tuberculosis is not always specific and reliable, because other chest diseases can also appear similar to tuberculosis on an X-ray and in early stages of TB patient may not have any radiological evidence of TB.

“Chest X-rays can play a significant role in shortening delays in diagnosis. Furthermore, avoiding films by using digital Chest X-ray is an important advantage and Digital technology has a potential to solve most CXR problems

“Limitations on the wider use of chest X-rays, such as non-availability at peripheral health facilities, relatively high cost of radiological examination and the difficulty of interpreting results, even by trained physicians, need to be addressed.”

4.4. RECOMMENDED TB DIAGNOSTIC APPROACHES AND DIAGNOSTIC ALGORITHM FOR PASSIVE CASE FINDING

4.4.1. DIAGNOSIS OF PULMONARY TUBERCULOSIS

All patients suspected of having pulmonary tuberculosis should be carefully assessed for

- Presumptive TB in adults not at risk of having drug resistant TB
- Presumptive TB case at risk of having drug resistant tuberculosis (history of previous treatment, DR contact, new cases who failed to convert negative to end of intensive phase)
- Presumptive TB case who is vulnerable to have severe form of tuberculosis (HIV+, other immune-suppressed, seriously ill, hospitalized).
- Presumptive TB cases in Children and adults with difficulty in expectorating sputum or in cases where bronchial specimen has been collected using special procedure (Gastric aspirate, BAL, Bronchial biopsy).

Diagnosis of Pulmonary TB (PTB) in adults (No Known risk of DRTB).

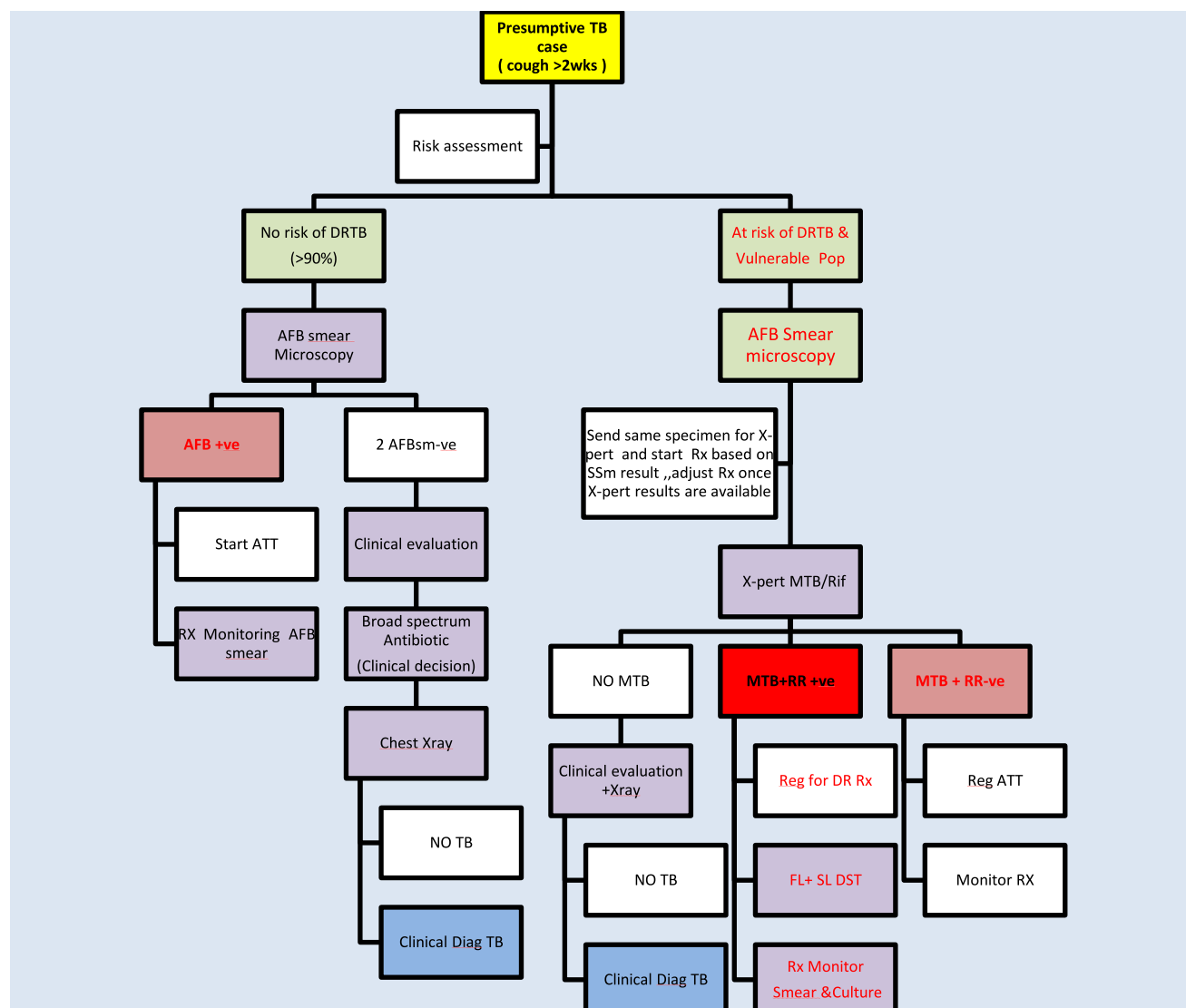
All adult patients suspected of having pulmonary TB should have at least two sputum specimens examined for AFB smear microscopy in a quality-assured laboratory (ISTC standard-2). All persons with chest radiographic findings suggestive of TB should also submit sputum specimens for microbiological examination (ISTC Standard 4).

The two sputum specimen should be collected as follows

- **Spot Specimen:** Sputum sample is collected on same day as first consultation
- **Early morning Specimen:** Sputum sample is collected early morning at home next day after consultation.

Note: *If positive sputum smear result is reported before collection of second specimen then patient can be started on appropriate ATT without need for testing of second specimen*

Figure 1: Flow diagram for diagnosis of pulmonary tuberculosis



When possible, at least one early-morning specimen should be obtained, as sputum collected at this time has the highest yield. However, “**Same Day Diagnosis**” approach is recommended in situation where patient has travelled long distance to reach health facility or in chest camps or other special situation (active case finding), two sputum specimens may be collected (with one-hour gap) and examined on the same day (also known as front loading technique). For details Please refer to section “TB in special situations”.

Based on the microscopy results, pulmonary TB cases are classified as **Sputum smear positive TB patient** (Bacteriological positive B+ive) and **Sputum smear negative TB patient (clinical diagnosed)** (see Chapter 3 for definition). Smear-positivity and grade indicates relative bacterial burden and correlates with disease presentation

Diagnosis of Pulmonary TB (PTB) in children:

It is recommended that X-pert MTB/Rif should be used as initial test in preference to conventional microscopy and culture in all children suspected of having tuberculosis

- a. These recommendations apply to the use of X-pert MTB/Rif in processed and unprocessed sputum specimens.
- b. These recommendations also apply to gastric lavage and aspirates.
- c. Children suspected of having pulmonary TB but with a single X-pert MTB/Rif negative result should undergo further diagnostic testing, and a child with high clinical suspicion for TB should be treated even if an X-pert MTB/Rif result is negative or if the test is not available

Diagnosis of Pulmonary TB (PTB) in Vulnerable Population Patient living with HIV:

Use of X-pert MTB/Rif is recommended as preferred initial diagnostic test rather than conventional microscopy and culture in HIV +ve patients suspected of having TB.

X-pert MTB/Rif is also recommended as preferred test in other presumptive TB patient with compromised immunity, in seriously ill and hospitalized patients.

Diagnosis of Pulmonary TB (PTB) s in patient at risk of DRTB

X-pert MTB/Rif should be used rather than conventional microscopy and culture as the initial diagnostic test in children suspected of having MDR TB or HIV-associated TB. Following group of patient are considered at risk of drug resistant tuberculosis

- Presumptive /PTB case with history of previous anti-TB treatment. All retreatment cases should be screened for Rifampicin resistant using X-pert MTB/Rif assay at start of treatment.
- All MDR contact should be screened for TB and Rifampicin resistant simultaneously.

Note: For all patient group where X-pert /MTB Rif assay is recommended as preferred tool, it is recommended that for facilities where X-pert testing is not available on site and specimen requires transportation to higher level laboratory, smear microscopy should be then being performed in local laboratory and same specimen transported to X-pert site. While X-pert results are awaited, patient should be managed based on microscopy/clinical diagnosis.

4.4.2. DIAGNOSIS OF EXTRA-PULMONARY TUBERCULOSIS

Diagnosis of tuberculous meningitis: It is recommended that X-pert MTB/Rif should be used in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid specimens from children (and adults) suspected of having TB meningitis

For CSF specimens, X-pert MTB/Rif should be preferentially used over culture if the sample volume is low or additional specimens cannot be obtained, in order to reach quick diagnosis. If sufficient volume of material is available, concentration methods should be used to increase yield

Diagnosis of Extra pulmonary TB at other sites: X-pert MTB/Rif may be used as a replacement test for usual practice (including conventional microscopy, culture, and/or histopathology) for testing of specific non-respiratory specimens (lymph nodes and other tissues) from patient (adults +children) suspected of having extra pulmonary TB.

- Patient (adults and Children) suspected of having extra pulmonary TB but with a single X-pert MTB/ RIF-negative result should undergo further diagnostic testing, and those with high clinical suspicion for TB should be treated even if an X-pert MTB/Rif result is negative or if the test is not available.
- Pleural fluid is a suboptimal sample for the bacterial confirmation of pleural TB, using any method. A pleural biopsy is the preferred sample. The sensitivity of X-pert MTB/Rif in pleural fluid is very low. Nevertheless, any positive X-pert MTB/ RIF result based on pleural fluid should be treated for pleural TB, while those with a negative X-pert MTB/Rif result should be followed by other tests.
- These recommendations do not apply to stool, urine or blood, given the lack of data on the utility of X-pert MTB/Rif on these specimens

Other test for diagnosis of Extra-pulmonary specimen: Number of bacilli in EPTB specimen (tissue, biopsy, pus, urine) is much lower compared to sputum, as a result diagnostic yield of AFB smear is also low in extra-pulmonary specimen. However, AFB microscopy should be attempted for diagnosis of TB in clinical specimen in situation where access to more sensitive diagnostic tools is not available.

Depending on the organ involved, diagnosis of extra-pulmonary tuberculosis can only be made based on positive X-pert/MTB. AFB smear or mycobacterium (MTB) culture or cytological/histological finding consistent with tuberculosis (caseating granulomas) and/or clinical/radiological evidence of active extra-pulmonary tuberculosis.

4.5. RECOMMENDED APPROACHES FOR SYSTEMATIC SCREENING FOR ACTIVE TUBERCULOSIS

The primary objective of screening for active TB is to ensure that active TB is detected early and treatment is initiated promptly, with the ultimate aim of reducing the risk of poor treatment outcomes, health sequelae and the adverse social and economic consequences of TB, as well as helping to reduce TB transmission^[12].

However, while the systematic reviews show that there is some evidence that screening can improve the early detection of TB, the direct evidence remains weak for the impact of screening on health outcomes and TB transmission when compared with passive case-finding alone. Furthermore, data

are lacking on the cost effectiveness of screening compared with other interventions to improve early detection, and it is clear that indiscriminate screening can require a lot of resources. Decisions on when and how to screen for active TB, which risk groups to prioritize and which algorithm to use for screening and diagnosis would depend on the epidemiological situation, the capacity of the health system, and the availability of resources.

Key principles for systematic screening for active TB

The following key principles should be considered when planning a TB screening initiative.

1. Before screening is initiated, high-quality TB diagnosis, treatment, care, management and support for patients should be in place, and there should be the capacity to scale these up further to match the anticipated rise in case detection that may occur as a result of screening.
2. Indiscriminate mass screening should be avoided. The prioritization of risk groups for screening should be based on assessments made for each risk group.
3. The choice of algorithm for screening and diagnosis should be based on an assessment of the accuracy of the algorithm for each risk group considered, as well as the availability, feasibility and cost of the tests.
4. TB screening should follow established ethical principles for screening for infectious diseases, observe human rights, and be designed to minimize the risk of discomfort, pain, stigma and discrimination.
5. The TB screening approach should be developed and implemented in a way that optimizes synergies with the delivery of other health services and social services.
6. A screening strategy should be monitored and reassessed continually to inform re-prioritization of risk groups, re-adaptation of screening approaches when necessary and discontinuation of screening at an appropriate time.

Recommendations on risk groups to screen

Seven recommendations on prioritizing risk groups for screening have been developed including three strong and four conditional recommendations.

Three **strong recommendation** is one for which the desirable effects of adhering to the recommendation are judged to clearly outweigh the undesirable effects and for which screening is judged feasible, acceptable and affordable in all setting and include 1) Household and other close contacts of TB patients 2) people living with HIV at each visit to health facility 3) Current and former workers in workplaces with silica exposure.

A **conditional recommendation** is one for which the desirable effects of adhering to the recommendation probably outweigh the undesirable effects and includes four recommendations for systematic screening of four groups 1) prisons and other penitentiary institutions, 2) people with an untreated fibrotic chest X-ray lesion 3). People who are seeking health care or who are in health care and who belong to selected risk groups (underweight, old age, diabetics, COPD) 4) subpopulations that have very poor access to health care, such as people living in urban slums, homeless people, people living in remote areas with poor access to health care, and other vulnerable or marginalized groups including some indigenous populations, migrants and refugees.

Algorithms for screening and diagnosis

Different screening algorithm options have been developed for adults and children. Options for the initial screening include screening for symptoms (screening either for cough lasting for longer than 2 weeks, or screening for any symptom compatible with TB, including cough of any duration, haemoptysis, weight loss, fever or night sweats) or screening with chest radiography. If symptom screening is used initially, then chest radiography can be used as a second screen to improve the pre-test probability of the subsequent diagnostic test, and to reduce the number of people who need to undergo further diagnostic evaluation.

The algorithms have different costs, and requirements in terms of human resources and health systems. The choice of algorithm for screening and diagnosis depends on the risk group, the prevalence of TB, the availability of resources and feasibility.

Recommendation for Systematic screening for active tuberculosis in Pakistan

NTP recommends systematic screening for active tuberculosis.

- Health facilities /communities for House hold and other Contact of smear-Positive tuberculosis in routine practices
- Special health care facilities (HIV surveillance sites) for patient living with HIV.
- Communities that have very poor access to health care, such as people living in urban slums, homeless people, people living in remote areas with poor access to health care, and other vulnerable or marginalized groups including some indigenous populations, migrants and refugees through special organized chest camps.
- Special health care facilities for screening of Tuberculosis in diabetics, chronic obstructive pulmonary disease and pregnant females.

Symptomatic screening for active tuberculosis in contact of TB patients

Contacts of tuberculosis patients are at high risk of infection and of developing tuberculosis, justifying active case detection in these individuals. It is recommended that contact investigation be conducted for house hold and close contacts when

INDEX CASE IS

- Sputum smear-positive pulmonary TB,
- Multi-drug-resistant TB (MDR-TB or extremely-resistant TB (XDR-TB)
- PLHIV or
- Child < 5 years of age

CONTACT HAS/IS

- Symptoms suggestive of TB (all ages),
- Child < 5 years of age,
- Known or suspected immune-compromising conditions (especially PLHIV)
- Contacts of MDR-TB or XDR-TB.

CHAPTER 5

TREATMENT OF TUBERCULOSIS

5.1. PRINCIPLES OF TREATMENT

TB is a curable disease if treated with quality assured anti-TB drugs in proper dose and duration. It not only carries the individual benefit by curing TB patients but also induces the epidemiological impact by cutting the chain of transmission effectively. The following four principles must be followed:

5.1.1. Anti - TB drugs must always be given in combinations

Large bacterial populations contain a small proportion of abnormal bacilli (mutants) that are not susceptible to any particular one or two drugs prior to their administration. When such a population is exposed to 1 or 2 drugs, the sensitive bacteria are killed; the non-susceptible bacteria survive, subsequently multiply and replace the susceptible bacterial population leading to drug resistance. When patient is treated during the intensive phase with four anti TB drugs the majority of bacterial population including mutant bacilli is killed. Subsequently, the patients can be safely treated with 2-3 drugs during the continuation phase, depending on the category of the patient.

5.1.2. Drugs should be prescribed in correct dosages

The tubercle bacilli are killed only when anti TB drugs are given in correct dosages. Under-dosage of drugs leads to resistance.

5.1.3. Anti-TB drugs should be taken for defined duration (based on categories)

In bacterial population, bacteria grow at different rates and intervals. However, studies have proven that 6months treatment is adequate and there are minimal chances of relapse.

5.1.4. Anti TB drugs preferably be taken with empty stomach on a regular basis

Irregular treatment leads to resistance and for the proper absorption of anti-TB drugs taking them empty stomach should be preferred. .

5.2. STANDARDIZATION OF TREATMENT

To avoid under treatment acquired drug resistance, side effect of over-treatment and to maximize cost-effective use of resources, standardized treatment (Fixed dose combinations) regimen to the diagnostic category has been recommended. The standardized regimens have the following advantages over individualized prescription of drugs:

- Reduces errors in prescription thereby reducing the risk of development of drug resistance.
- Facilitates estimation of drug needs, purchasing, distribution and monitoring.

- Facilitates staff training.
- Reduces the cost.
- Facilitates regular drug supply when patients move from one area to another.

To ensure prescription of standardized regimens the patients have been divided in various types and categories.

5.3. CATEGORIES OF TB PATIENTS

The categorization of patients in two categories is based on type of patients and sputum results.

New cases (Category-I): This includes a) new cases of pulmonary TB. b) new extra-pulmonary TB.

Re-treatment cases (Category-II): This includes relapses, treatment after failure, and treatment after loss to follow-up, others previously treated (positive & negative) & patients with unknown previous TB treatment history.

Note: For the purpose of treatment, Cat-I&II will be used in Record and Reporting tools to differentiate the treatment regimen.

5.4. DRUGS AND REGIMENS

Prescribing standardized drug regimen according to the category of a diagnosed patient is the responsibility of the clinician at the Basic Management Unit (BMU). TB patients must be treated with the anti-tuberculosis drug regimens recommended by NTP/PTP Pakistan. The NTP/PTP recommended drug regimens are very effective and can treat successfully almost all cases of tuberculosis if used in the right dosage and for the right duration. Currently the treatment period for new TB cases lasts 6 months and for re-treatment cases is 8 months. The five essential anti-TB drugs used in the NTP Pakistan, with their mode of action and dosage (in mg per kg body weight), are given in the table below.

Uninterrupted availability of ATT drugs must be ensured to every TB patient free of cost and compliance of patient to complete treatment should also be ensured. The most important drugs used in the treatment of Tuberculosis are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Streptomycin (S), and Ethambutol (E). Fixed dose combinations with proven bio-availability are preferred over individual drugs preparations. The quality of anti-Tuberculosis drugs should be ensured through regular and random testing of batches of drugs after procurement as well as after being stored under field conditions for specified periods. The use of Rifampicin or Streptomycin, for diseases other than mycobacterial diseases, should be avoided or limited to very carefully considered indications.

5.4.1. TREATMENT REGIMEN FOR CATEGORY I (NEW CASES)

During the initial intensive phase, a combination of four drugs (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol “HRZE”) are administered under observation daily for a period of two months (sixty doses). When the patient has completed the initial intensive phase of two months, first follow up sputum test is done, and continuation phase will start irrespective of sputum smear result. Similarly,

for smear negative cases initial intensive phase (HRZE) is administered for two months. Sputum smear is done at the end of 2 months, if smear is negative, the continuation phase will start. However, if sputum smear is positive, *it will be tested on X-pert and if test result is Mycobacterium detected but RR not detected patient, continuation phase will start.* During the continuation phase, isoniazid and Rifampicin (HR) are administered daily for four months.

Note: Rifampicin-containing regimens should be taken under direct observation.

5.4.2. TREATMENT REGIMEN FOR RE-TREATMENT CASES (CATEGORY II):

Note: After registration as re-treatment case & before starting treatment, all cases eligible for re-treatment regimen will be tested on X-pert to exclude RR.

During the initial intensive phase Rifampicin, Isoniazid, Pyrazinamide and Ethambutol, supplemented with streptomycin (HRZES) are given for the first two months, followed by the same drugs without streptomycin (HRZE) for another one month administered daily under observation. The initial intensive phase should be continued for three months. If the sputum smear is negative at the end of 3rd month, the continuation phase is started. If the sputum smear is positive at the end of 3rd month, X-pert test will be repeated. If RR is detected patient will be shifted to DR register and if RR is not detected the patient should then start the continuation phase.

During the continuation phase, Isoniazid, Rifampicin, and Ethambutol (HRE) are administered daily for five months under observation. If the patient remains smear-positive after the end of five months, he/she is no longer eligible for the re-treatment regimen. Such patients are regarded as CAT-II treatment failure & refer to PMDT unit as MDR presumptive cases.

5.5. DOSAGE AND DURATION OF TREATMENT

Prolonging treatment beyond the recommended period of 6 months has minimal benefits provided the patient has taken the medication without interruption. Anti-TB drugs may need to be temporarily suspended or stopped in case of severe drug intolerance or toxicity.

The dosages of fixed dose combination and individual drugs for each category of treatment are given in the tables below:

Table 2: Regimen: New cases (Category – I) dosages with fixed-dose combinations in adults

Patient body Weight (kg)	Initial intensive phase daily (2 months)	Continuation Phase daily (4 months)	
	HRZE (H 75mg + R 150 mg + Z 400mg + E 275mg)	HR (H 75mg + R 150mg)	HR ² (H 150mg+ R 300mg)
30-39	2	2	1
40-54	3	3	1.5
55 and above	4	4	2

² If RH (R 150mg + H 75mg) is not available, then use RH (R 300mg + H 150mg)

Table 3: Regimen: Re-treatment (Category – II) dosages with Fixed-dose combinations in adults

Patient body Weight (kg)	Initial intensive phase daily (3 months)		Continuation Phase daily (5 months)
	HRZE (H 75mg + R 150 mg + Z 400mg + E 275mg)	Streptomycin (750mg) (only for initial 2 months of intensive phase)	HRE ³ (H 75mg +R 150mg + E 275mg)
30-39	2	500 mg	2
40-54	3	750 mg	3
55 and above	4	750 mg	4

(H = Isoniazid, R = Rifampicin, Z = Pyrazinamide, E= Ethambutal, S= Streptomycin)

³ If HRE (H 75 mg + R 150 mg + E 275 mg) is not available, then use separate HR (H75mg +R150 mg) + E (E 400 mg)

CHAPTER 6

MANAGEMENT OF CONTACTS & USE OF INH PROPHYLAXIS

6.1. MANAGEMENT OF CONTACTS

Tuberculosis (TB) contacts are people who are in close contact with patients with infectious TB. As they are at high risk for TB, so needs to be investigated systematically and actively for TB infection and disease.

Contact investigation contribute to increase number of TB cases by early identification of active TB, thus decreasing its severity and reducing transmission of *Mycobacterium tuberculosis* to others and identification of latent TB infection (LTBI) to allow preventive measures. Many studies in countries with a high TB incidence have shown that the prevalence may reach 5% or more among contacts, particularly among household members of bacteriologically positive cases.

Contact investigations could be particularly useful for identifying childhood TB. Furthermore, it can help identify people who require careful follow-up, such as those who were exposed to an index case of multi-drug-resistant or extensively drug-resistant TB or people infected with HIV, and among those having risk for rapid progression to active TB is very high.

National TB control Program recommends that contact investigation be conducted for household and close contacts when the index case has any of the following characteristics:

- ✓ has sputum bacteriologically positive pulmonary TB,
- ✓ has multi-drug-resistant TB (MDR-TB or extremely-resistant TB (XDR-TB) (proven or suspected);
- ✓ Is a People Living with HIV (PLHIV); or
- ✓ Is a child < 5 years of age?

In addition, Program recommends that contact investigation be conducted for household and close contacts of all other index cases with pulmonary tuberculosis

Children <5 years of age who are household or close contacts of people with TB and who, after an appropriate clinical evaluation, are found not to have active TB should be treated for presumed LTBI as per following guidelines.

The management of household contacts consists of the following two steps:

STEP 1: Interview with the patient to identify the adults and children (older than 5 years of age) with symptoms suggestive of tuberculosis. All symptomatic contacts should be called to visit the Basic Management Unit (BMU) at their earliest convenient date for investigation. The patient is explained the importance of contact screening to bring the household members to get screened. The contacts are subjected to sputum examination in-line with NTP recommendations.

STEP 2: All children less than 5 years of age should be brought to the BMU for further assessment and management, irrespective of symptoms.

The NTP has given the policy for contact management, tools and guidelines are available, but implementation at the grassroots level can be more effective if following challenges are addressed:

1. Social stigma: confidentiality, acceptance of own disease and potential denial among the symptomatic contacts (family elders, women, etc.).
2. Access: scattered population and limited access to facilities, and cost implications.
3. Time consuming: over burden facility, limited time available with the health care provider to interview and convince the index case.

The table below illustrate the protocol for management of contact:

Table 4: Management of close contacts

CLOSE CONTACT	SCREENING	ACTION
Adult	Chest symptoms (Cough > 2 weeks or other TB symptoms)	Do sputum smears / other investigation if needed
Child	No symptoms	<ul style="list-style-type: none"> - Reassure and check for BCG scar - Give BCG, if not already given - Prescribe INH in a dosage of 10 mg/kg body weight for a period of six months, if age of child contact is 5 years or below
	With symptoms	Refer to specialist for evaluation
Child breast fed by Smear-positive mother		<ul style="list-style-type: none"> - Treat the mother - Protect the child with INH 10 mg. /kg. for 6 months - Continue breast-feeding - At completion of 6 months, give BCG, if not already given.

6.2. CANDIDATES FOR IPT (INH PROPHYLAXIS TREATMENT)

- The children below 5 year of age and are close contact of Bacteriologically Positive (B+ive) TB patient, are put on INH prophylaxis therapy (IPT). The INH is prescribed in a dosage of 10 mg/kg and is given for a period of 6 months.

- Child breast-fed by B+ive mother would continue to breast feed. The child should be protected by prescribing INH in same dosage for six months and is given BCG at end of six months, if not already given.

Note: The rationale for assigning high priority to contacts of index cases < 5 years of age is to find the source of the infection. Children 5 years and below are at higher risk for acquiring TB infection and of progressing from infection to TB disease.

- * HIV-positive with no active TB household or close contacts
 - ✓ HIV-positive household or close contacts who are adults or adolescents and whose clinical evaluation suggests that they are unlikely to have active TB should receive preventive treatment with isoniazid at 300 mg/day for at least 6 months. It is conditionally recommended that the duration of isoniazid preventive treatment of PLHIV with no active TB be prolonged to 36 months.
 - ✓ HIV-positive household or close contacts who are children with no active TB should receive preventive treatment with isoniazid at a dose of 10 mg/kg body weight for 6 months.
 - ✓ A 9-month regimen of daily INH is considered the optimal treatment for HIV-infected adults with Latent TB infection (LTBI). To be considered adequate therapy, the patient must receive a minimum of 270 doses of INH administered within 12 months. HIV-infected children should receive 9 months of INH treatment for LTBI. To be considered adequate therapy for HIV-infected persons, twice-weekly regimens of INH must be administered by DOT and consist of at least 76 doses administered within 12 months.

CHAPTER 7

MONITORING TB TREATMENT

To assess the progress of anti-TB drugs, patients are monitored at regular intervals through:

- 1) follow-up sputum smear examinations; and
- 2) checking the regularity of drug intake

Sputum should be examined at the end of the intensive phase of treatment i.e. at 2 months for New TB patients and at 3 months for Retreatment patients to assess the treatment progress. Sputum should also be examined at 5 months to assess the effectiveness of treatment for pulmonary smear-positive patients. For smear-negative cases, sputum should be examined once at the end of 2 months and at 5 & 6 months if smear-negative patient turns out to be positive at month 02 but RR not detected to ensure that these patients remain smear-negative. For monitoring purposes, one sputum smear examination during the above specified months is sufficient.

Observed treatment is required for entire duration of treatment in both New and Retreatment cases to avoid the risk of drug resistance. The patient and treatment supporter will be educated accordingly and will be advised to maintain treatment supporter card for entire duration of treatment and collect drugs in presence of treatment supporter on monthly basis throughout the full duration of treatment.

Table 5: Sputum smear examination schedule according to classification of TB patient

Category of Patient	AFB smear examination		Management
	Month	Result	
New Bacteriologically positive	0Months	Positive	START treatment intensive phase (2HRZE)
	End of 2Months	Negative	START continuation phase treatment (4HR)
		Positive	Do X-pert test. If RR not detected. START continuation phase treatment .If RR detected then refer to PMDT site for Management of (DR-TB).
	End of 5Months	Negative	Continue treatment
		Positive	Declare treatment outcome as CAT-1 TREATMENT FAILURE For further management refer protocol for cat-II
	End of 6Months	Negative	Stop treatment and declare treatment outcome- If last sputum not done, declare treatment completed
		Positive	Declare treatment outcome as CAT-1TREATMENT FAILURE For further management refer protocol for cat-II

New Bacteriologically Negative	0Month	Negative	Start intensive Phase 2HRZE
	End of 2Months	Negative	Start continuation phase treatment 4RH
		Positive	Do X-pert test ,if RR not detected, start continuation phase and continue the follow up as in Category 1(Smear positive)
All retreatment cases after failure, lost to follow up or relapse	0Months	Positive	Register patient for Cat-II
			Do X-pert before start of treatment refer patient /transport specimen for X-pert testing If R resistant refer to the DR TB management unit If R sensitive, Start intensive Phase (2HRZES 1HRZE).
	End of 3Months	Negative	Start continuation phase treatment (5RHE)
		Positive	Repeat X-pert test- if DST available send specimen for DST also. If X-pert report as RR refer patient to PMDT site for management If RR not detected start continuation phase of re-treatment.
	End of 5Months	Negative	Continue continuation phase
		Positive	Declare Treatment outcome CAT-II TREATMENT FAILURE Declare MDR presumptive case. Refer Patient to DRTBMU
	End of 8Months	Negative	Declare treatment outcome “ CURE”
		Positive	Declare Treatment outcome CAT-II TREATMENT FAILURE Declare MDR presumptive case. Refer Patient to DR-TBMU

7.1. TREATMENT OUTCOMES

- The BMU will declare treatment outcome for registered TB patients on quarterly basis, based on the data recorded in TB01 card & TB03 register.
- The NTP has given definitions for various treatment outcomes of the TB patients. The definitions used are compatible with international suggestions.
- The treatment outcomes are explained in some detail in table below:

Table 6: Treatment outcomes

Cured	A patient registered as smear-positive, has completed the duration of treatment, and becomes sputum smear negative at the end of treatment and on at least one previous occasion.
Treatment completed	A smear positive patient who has completed the duration of treatment and have at least one follow up smear negative results but none at the end of treatment due to any reason
	Smear negative and extra pulmonary cases complete six months of treatment successfully
Treatment failure	A sputum smear positive patient who remains or becomes sputum smear positive at month five or later.
Died	A patient who dies for any reason during the course of treatment.
Lost to follow up	A patient whose treatment was interrupted for two consecutive months or more after registration
Not evaluated	A TB patient for whom, no treatment outcome is assigned (includes “Transfer out” to another treatment unit and whose treatment outcome is unknown).

7.2. DIRECTLY OBSERVED TREATMENT (DOT)

Regular supervision is required to ensure that the patient takes all the drugs prescribed. Direct observation may be ensured through the following:

- Providing treatment services as close to the patient's home as possible; the patients should receive every dose of treatment under the direct supervision of a treatment supporter, observing the patients swallowing all tablets.
- The importance of regular drug intake and treatment completion should be emphasized on the patients and their relatives through a counselling session.
- NGOs can also play an important role in this regard by enhancing patient education and community assistance.
- The NTP has developed a detailed strategy to observe community-based DOTS at all BMUs and treatment centres in the country. The key features of this strategy are summarized below:
 - o The patient selects the health facility usually a BHU for weekly visit for management of side effects if any, selection of treatment supporter and consultation/referral of contacts.
 - o If any health facility is not near to his/her home, he will select a treatment supporter who will observe the daily intake of drugs at a mutually agreed place.

- The treatment supporter identified by the patient will be briefed by the DOTS facilitator at the health facility for observing the intake of drugs.

The treatment supporter accompanied by patient will collect the drugs on monthly basis from BMU where patient is registered throughout full course of treatment

- Patients are referred to the BMU for follow-up sputum examinations at the end of months 2, 5 and 6 and the sputum results recorded in TB-01 & TB03. In Cat-I and at end of months 3, 5 and 8 months for Cat-II cases.

7.3. FOLLOW-UP AFTER COMPLETION OF TREATMENT

Subsequent relapse is rare when patients complete the prescribed course of chemotherapy. It is therefore unnecessary to follow patients who have completed their treatment and who have been declared cured. Patients who have completed their treatment should, however, be told to report for re-examination if symptoms recur and the procedure described under "Diagnosis of Tuberculosis", should then be followed.

7.4. RETRIEVAL OF DELAYED PATIENTS

If a patient misses his/her treatment for more than 2 consecutive days during the intensive phase, he/she must be reminded on cell phone/SMS, if no response, will be traced by health workers or by the treatment supporter. Every effort should be made to educate the patient on the importance of adhering to his/her treatment schedule. During continuation phase of treatment, if patient fails to collect drugs within one week of drug collection day he must be reminded on cell phone/SMS, and if no response will be traced by health workers.

7.5. ROLE OF COUNCELING AND HEALTH EDUCATION IN TUBERCULOSIS

Counselling and health education should be provided to the health staff, patients and their relatives. It is often necessary to carry out such a counselling session for a patient in the presence of treatment supporter who will monitor his/her intake of drugs on a daily basis.

The general public need to be educated on the importance of early presentation at a health facility for those with chest symptoms, especially cough, persisting for 2 weeks or more. Patients with these symptoms should present themselves for a sputum examination as early as possible at the nearest health facility as delay in diagnosis leads to complication and death. In addition, efforts should be made to make people aware of the, fact that TB is curable with adequate treatment, but if not treated properly it will be converted into resistant form of disease which is very difficult to treat. Good communication between a patient and the health worker is also very important. Patients will be provided health education on continuous basis during treatment period so that he should understand the importance of regular in taking of all his prescribed drugs, duration of treatment and importance of sputum examination.

CHAPTER 8

ENGAGING ALL CARE PROVIDERS IN TB CONTROL

8.1. INTRODUCTION

In Pakistan, private sector is considered as the first point of contact in >75% of the patients with various type of ailments. As in most countries with a significant burden of TB, DOTS implementation is limited largely to public sector services under national tuberculosis Programs. However, it is a fact that many patients with symptoms of TB, including the very poor, do seek and receive care from a wide variety of health care providers outside the network of NTP services mostly not following National Guidelines. These include private providers (for profit and not-for profit e.g. GPs, private hospitals and NGOs) and other public sector institutions such as Army, Railway, Social Security, etc. Thus the TB patients they serve are not usually in the overall network of TB care services in the country and completely reported in the national TB case notification. Engaging all health care providers in TB control is an essential component of WHO new Stop TB strategy and the Stop TB Partnership's Global Plan to Stop TB 2006-2015, and is also a major component of Pakistan National TB Control Strategy: Vision 2020.

The NTP/PTP is in the process of consolidation and scaling up DOTS activities through several innovative approaches by engaging all care providers in order to standardized TB case management and reporting practices. There are few models currently exist under the Public-Private Partnership (PPP) and are contributing to case notification and treatment success. A fifth model is being proposed for involving informal health sector.

1. District led GP model: The model engages the solo GPs and labs in a district. However, the main stewardship is with the district health authorities and district TB coordinator has the pivotal role. All the TB related activities and implementation is done under the stewardship of the public sector. The intermediary body supporting the project has mainly a role of coordination between the GPs and the Public sector, providing logistics for the project and organizing community awareness activities.
2. NGO model: The model is experienced mainly in Punjab where Pakistan Anti TB association has a large network which mainly provide TB care, self-operated, supported by local philanthropists. The AKHSP is working in GB and MALC is operational with few centers in Sindh. The model gets technical and logistic support from district TB control Program
3. Large private hospitals model: Includes large private hospitals and private tertiary Care Hospitalising. (Gulab Devi and Indus Hospital). The large private hospitals are engaged with PTPs and gets technical and logistic support from district TB control Program which directly monitor the TB DOTS implementation, provides drugs & trainings, and generates quarterly reports e.g. Ghurki trust hospital, Bethania hospital etc.
4. Other public sector model: this include those public sector organizations which are not under department of health and have their own health care system for employees and families i.e. Army, Social Security, Fauji foundation, Wapda, Railways Cantonment board etc. The model gets technical and logistic support from provincial and district TB control Program.

PPP also implies engaging relevant care providers in prevention and management of childhood TB, MDR-TB and in the implementation of TB/HIV collaborative activities.

8.2. GUIDING PRINCIPLES

The PPP should be implemented under the following principals:

1. Training protocols
 - Context specific training modules and methodology for private sector should be implemented.
2. Diagnostic protocols
 - The national diagnostic algorithm for passive and active case finding shall be followed in private sector.
 - Sputum smear microscopy shall be considered as the core diagnostic tool for TB.
 - Latest diagnostic technologies shall be permissible, wherever available, with standard protocols recommended by NTP
 - TB Diagnostic facilities of public sector can be utilized by private sector where required.
3. Treatment protocols
 - The private sector shall follow the treatment protocols as mentioned in National TB guidelines.
4. Pharmaceutical and health products:
 - TB Program shall provide ATT and TB lab diagnostic supplies as per requirement, through its existing supply mechanism.
5. Recording and reporting protocols
 - Standard recording and reporting, adapted for private sector context, should be followed.
 - Electronic Nominal Reporting System (ENRS) should be followed.
6. Monitoring & supervision protocols
 - A strong integrated supervision and monitoring mechanism based on provision of technical support to the private sector shall ensure recording, reporting, dissemination and feedback mechanisms at operational site.
 - The provincial and district Public Private Partnership committees shall be responsible for the overall monitoring and supervision of all TB control activities in the private sector.
 - Context specific M&E tools shall be used

- Use of mobile applications and other innovative technologies shall be encouraged for monitoring & surveillance.

7. Incentives

- Incentives for private sector may be provided as per availability of resources in consultation with stake holders.

CHAPTER 9

MANAGING CHILDHOOD TUBERCULOSIS

9.1. BACKGROUND

Childhood TB is one of the major communicable diseases causing high morbidity and mortality among children in developing countries. Children are at higher risk for development of TB as compared to adult. Although the actual burden of cases is unknown, according to WHO most childhood TB cases are found in high TB burden countries. Latest WHO estimates from 2012 suggest 530,000 TB cases in the under 15 years of age demographic and 74,000 TB deaths worldwide, amounting to 6% and 8% of all TB respectively. Child TB may comprise 3-23% of the TB caseload in high TB burden countries. In Pakistan child TB comprises 10% of all notified TB cases.

9.2. STRATEGY TO CONTROL CHILDHOOD TB

Childhood TB care is an integral part of the ongoing routine DOTS implementation in the country. Currently the Childhood TB intervention has expanded to cover all 142 districts of the country up to the level of secondary facilities (i.e. district headquarter hospitals, tehsil/taluka hospitals). It is intended that this intervention will gradually be further expanded to include primary level facilities.

The childhood TB intervention has the following five main components:

- Adequate diagnostic facilities including sputum smear microscopy, culture & sensitivity, tuberculin skin testing, radiology, X-pert etc.
- Uninterrupted supply of anti-TB drugs for children where the Program has been implemented
- Training, supervision and monitoring of care providers involved in childhood TB management on National Paediatric TB Guidelines.
- Recording and reporting of childhood TB case management and outcomes.
- Education and treatment support for childhood TB cases.
- Management of child contacts and IPT provision for <5-year-old contacts of adult TB cases

9.3. DIAGNOSIS IN CHILDREN

Sputum samples are difficult to obtain from children. The diagnosis of tuberculosis in children rests largely on the results of clinical history, contact history usually with an infectious case within the family, X-ray examination (unilateral lymph-adenopathy and/or infiltration in lung fields), sputum microscopy and a positive tuberculin skin test where available. However, current WHO recommendations include preferential X-pert testing as an initial diagnostic test for all children suspected of having TB X-pert may also be used as a replacement test instead of usual practice (including conventional microscopy culture and/or histopathology) for the testing of non-respiratory specimens (lymph nodes and other tissues) from children suspected of having extra pulmonary TB.

Additionally, routine HIV testing is recommended for children with presumptive or diagnosed TB. The NTP Pakistan has developed and implemented its ‘guidelines for the management of childhood TB’ and also training materials. These materials include sections on the diagnosis and management of childhood TB. It also contains steps on the administration of tuberculin skin test.

The decision whether or not to treat the child should be made by a physician trained on the new NTP guidelines to manage childhood TB or by a specialist. The PPA scoring chart helps in evaluating probable TB on the basis of multiple features i.e. clinical, histological, radiological etc.

TABLE 7: SCORING CHART FOR THE DIAGNOSIS OF CHILDHOOD TB.

Condition	Scores				
	1	2	3	4	5
Age	< 2 years				
Close contact in last 2 years	TB patient S –ve		TB patient S +ve		
BCG scar	Absent				
Low immune status	Yes				
PCM grade-3	Yes		Not improve		
Physical examination findings		Suggest TB		Strongly suggest TB	
Chest X-ray	Non-specific	Suggest TB			
Tuberculin skin test	5 – 10 mm		> 10 mm		
Granuloma	Non-specific				TB
H/o measles & whooping cough in the last:	3 – 6 months	< 3 months			

Note: Attach the scoring chart with TB01

TABLE 8: INTERPRETATION OF SCORES

Score	Interpretation	Suggested Actions
0 – 2	Unlikely TB	Investigate other reasons of illness
3 – 4	Possible TB	-Do not treat for TB -Manage the presenting symptom(s) -Monitor monthly the condition(s) for 3 months, using scoring chart
5 – 6	Possible TB	-Investigate and exclude other causes of illness -Investigation may justify therapy
7 or more	Probable TB	- confirm (if possible)

9.4. PRINCIPLES OF TREATMENT IN CHILDHOOD TB

The principles of treatment of TB in children are the same as for the treatment of TB in adults. The main objectives of anti-TB treatment are to:

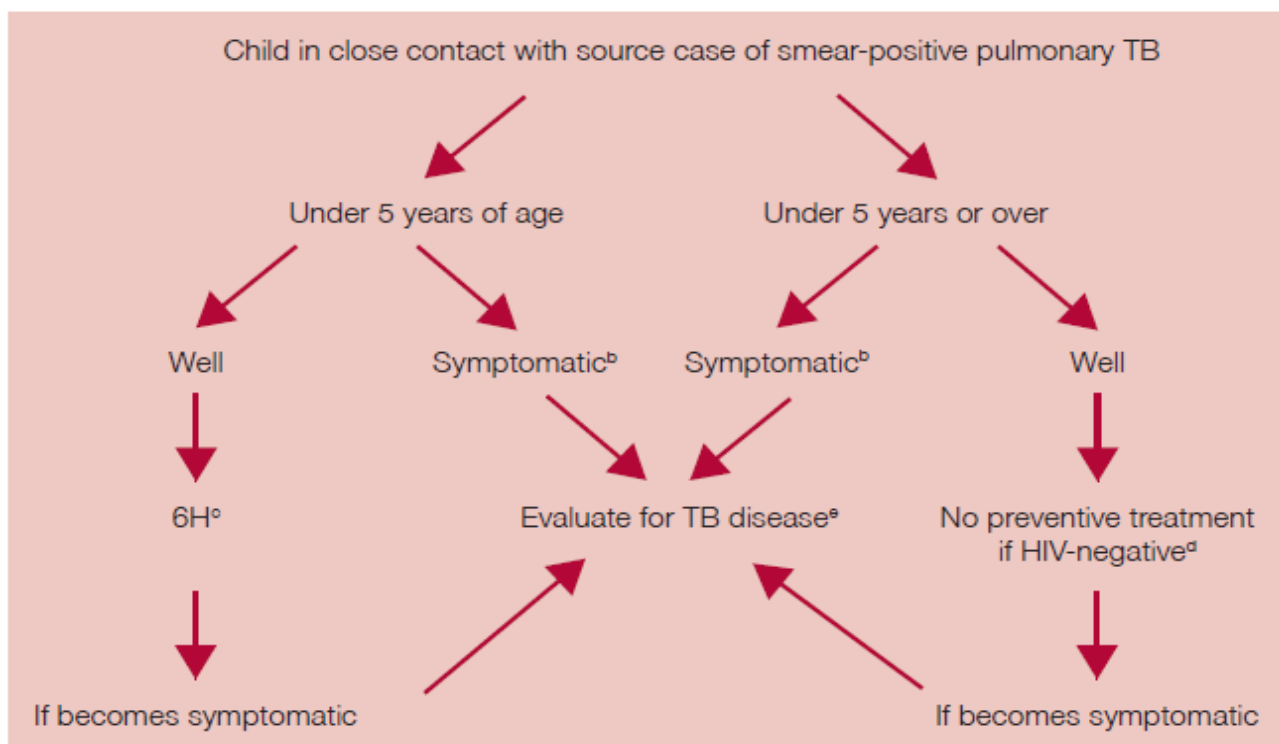
- cure the patient of TB;
- prevent death from TB disease or its late effects;
- prevent relapse of TB;
- prevent the development and transmission of drug-resistant TB;
- reduce transmission of TB to others;
- achieve all this with minimal toxicity.

All children treated for TB should be registered with the NTP.

9.5. CONTACT SCREENING & PREVENTION OF TB IN CHILDREN

The details have been described in the relevant section. Symptom based screening approach to child contact management is presented below which has been adapted from WHO guidelines.

Figure 2: Flow diagram for screening children for tuberculosis



9.6. ISONIAZID PREVENTIVE THERAPY

Preventive therapy is indicated for an asymptomatic contact or contact in whom TB disease has been excluded if the contact is less than 5 years of age or who is living with HIV. Preventive therapy for young children with TB infection who have not yet developed TB disease will greatly reduce the likelihood of TB disease developing during childhood.

- Children <5years of age who are household or close contacts of people with TB and who, after an appropriate evaluation, are found not to have TB disease should be given 6 months of IPT (10mg/kg per day, range 7-15mg/kg, maximum dose 300mg/day)

9.7. TREATMENT OF CHILDHOOD TB

The section below has been adapted from the recent WHO childhood TB guidelines 2014.

Table 9: Drug Regimens

Recommended daily dose for 1st line anti-TB drugs for children		
Anti TB drugs	Dose an range (mg/kg body weight)	Maximum dose (mg)
Isoniazid	10 (7-15)*	300
Rifampicin	15 (10-20)	600
Pyrazinamide	35 (30-40)	-
Ethambutol	20 (15-25)	-
* The higher end of the range of isoniazid dose applies to young children; as the children grow older the lower end of the dosing range becomes more appropriate		

Table 10: Treatment Regimens

RECOMMENDED TREATMENT REGIMENS FOR TB IN CHILDREN		
TB diagnostic category	Anti-TB drug regimens ^a	
	Intensive phase	Continuation phase
<i>Low HIV prevalence (and HIV-negative children) and low isoniazid resistance settings ^b</i>		
<ul style="list-style-type: none"> - Smear negative pulmonary TB - Intrathoracic lymph node TB - Tuberculosis peripheral lymphadenitis 	2HRZ	4HR
<ul style="list-style-type: none"> - Extensive pulmonary disease - Smear-positive pulmonary TB - Severe forms of extra-pulmonary TB (other than tuberculous meningitis/ osteoarticular TB) 	2HRZE	4HR
<ul style="list-style-type: none"> - Tuberculous meningitis and osteoarticular TB 	2HRZE ^c	10HR

- a. The standard code for anti-TB treatment regimens uses an abbreviation for each anti-TB drug: isoniazid (H), Rifampicin (R), pyrazinamide (Z) and ethambutol (E). A regimen consists of two phases – the initial and continuation phases. The number at the front of each phase represents the duration of that phase in months. Example, 2HRZ: Duration of this phase is 2 months and drug treatment is daily (no subscript numbers after the abbreviations) with isoniazid, Rifampicin and pyrazinamide.
- b. See “Definitions and distinctions” section for discussion of WHO definitions of high and low prevalence of HIV and isoniazid resistance.
- c. The decision on the regimen for a child with tuberculous meningitis should be made by an experienced clinician. It is suggested that the patient be treated in a hospital.

The WHO has recommended very recently that Streptomycin should not be given to children as a first line of treatment. H=Isoniazid, R=Rifampicin, Z=Pyrazinamide, E=Ethambutol

- Ethambutol can be used in children under 5 Kg under special circumstances recommended by the paediatrician. In the children over 5 Kg, arrange regular visual acuity and red-green discrimination checks. If any change, stop the drug.
- Streptomycin should not be used as part of first-line treatment regimens for children with pulmonary tuberculosis or tuberculous peripheral lymphadenitis.

CHAPTER 10

TUBERCULOSIS CARE IN HOSPITALS

Hospitals, mainly tertiary care hospitals (TCHs) and to some extent secondary level hospitals are the largest and best equipped health facilities in Pakistan's health system. This element was capitalized upon by adding various intervention in these hospitals including childhood TB (CTB), managing difficult to diagnose TB and TB/HIV co-infection. There are about 48 TCHs in the country and about 140 secondary (*District Headquarter Hospitals*) in the country, so there is a huge potential to offer specialist and routine care to the TB patients through these facilities.

It should be noted that the prerequisites of establishing the linkage in a hospital setting automatically entails an element of capacity building. These prerequisites pertain to capability of hospital laboratory facilities, capacity to handle the logistics related to the intervention, commitment to providing human resource and facilitating the intervention. Beyond this hospital linkage being implemented can be envisaged as incorporating the following components:

1. Internal Network/Hospital Coordination Mechanism - To identify and refer presumptive TB cases to the DOTS centre, and/or manage TB cases according the NTP's standardized guidelines; thus reducing "missed" cases.
2. External Network - To refer patients to peripheral BMUs & vice versa; easing accessibility and reducing loss to follow up cases at TCH / BMU requesting for eX-pert opinion in difficult cases. It is expected that this will help in reducing 'loss to follow up'
3. Reporting & Monitoring - To monitor implementation and provide data for Program improvement

Patients arriving at the hospitals may present with concomitant TB which might be missed when treating the primary ailment. When detected current management guidelines are not necessarily followed and detected cases may not be reported to NTP either. The intervention in the hospital is to sensitize the key hospital staff on NTP's standardized guidelines, thereby assisting in identifying presumptive TB cases and defining the mechanism by which such patients may be referred to the DOTS centre allowing increased enrolment at the DOTS centre. It further seeks to ensure that current standardized diagnostic and treatment practices, as advised by the NTP, are mainstreamed in the hospital setting. Meanwhile, the external network will ensure that enrolled patients remain on treatment by referring them to a management facility nearest to their place of residence. Breaks in treatment due to patient unavailability in hospital due to extended treatment time or travel constraints due to distant place of residence may be minimized by offering case management to be carried out locally, thus reducing accessibility issues. It is expected that this will assist in reducing 'loss to follow up' and 'default' cases, ultimately reducing the risk of MDR amplification. Apart from the application of NTP's standard R&R tools in these settings, a quarterly review meeting will review and recommend improvements for implementations.

CHAPTER 11

TUBERCULOSIS IN SPECIAL SETTINGS

11.1. TUBERCULOSIS IN PRISONS

Prison is a term used for any place of detention. It includes centers for pre-trial convicted prisoners as well as centers for juvenile offenders and illegal immigrants.

The estimated number of people detained on any given day, worldwide, is over 9 million. The turnover of prisoners (anyone under custody of the state) is high. On any given day, four to six times the estimated 9 million incarcerated persons pass through prisons.

Prisoners do not represent a homogenous segment of society. Many are poorly educated, and come from socioeconomically disadvantaged groups. They are young (15–44 years). TB rates of over 3,000 per 100,000, as compared to the general population, are not unusual. TB incidence rates are also extremely high in prisons, and TB mortality in prisons is elevated. The incidence of TB is approximately 50 times higher, and the mortality rate approximately 28 times higher, among prisoners than among the civilian population in these countries. An overwhelming majority is male; women prisoners represent less than 5 percent of the total prison population.

They may have unhealthy habits or addictions, such as alcoholism, smoking, and drug use, which contribute to their poor health and are risk factors for developing TB too. For these reasons, they enter prison already ill or with a higher risk of becoming ill compared to the general population.

11.1.1 Objectives for prison control. Why is TB in prisons important?

- Prisons act as a reservoir for TB, pumping the disease into the civilian community through staff, visitors and inadequately treated former inmates. TB does not respect prison walls.
- Improving TB control in prisons benefits the community at large. Community TB control efforts cannot afford to ignore prison TB.
- Prisoners have the right to at least the same level of medical care as that of the general community. Catching TB is not part of a prisoner's sentence.
- Drawing attention and resources to the problem of TB in prisons is likely to lead to an overall improvement in prison conditions, the health of inmates and human rights.
- The number of MDR-TB cases in prisons is often proportionally higher than that found in the general population of a given country.

11.1.2 SYSTEMATIC APPROACH TO INTRODUCING A TB CONTROL PROGRAM IN PRISONS

Advocacy and policy formulation: Baseline assessment of TB situation (epidemiology) and control practices in prisons Signed MOU for the collaboration for TB control in prisons group with terms of reference

Planning and Implementation

- Baseline assessment
- Standard Operating Procedures
- Prison-specific Recording and reporting tools
- Training and human and resource development
- Adapted NTP modules and training curricula
- National strategy for TB control in prisons
- Establishment of DOTS BMUs with quality assured Lab network
- Integration with district and provincial DOTS Programs (PDL mechanism).
- Surveillance system integrated with district and provincial TB Control Programs
- Infection control measures
 - a) Administrative control measures, including early TB case detection, TB Screening, separation or isolation of patients.
 - b) Collection of sputum in ventilated area.
 - c) Environmental control measures, including natural and mechanical ventilation
 - d) Personal protection control measures, including respirators

Detecting TB through Case Finding and Screening

- Passive Case Finding
- Active Case Finding
- Screening at entry to prisons
- Mass Screening
- Contact Screening

Contact Investigation: In congregate and overcrowded settings such as prisons, contact investigation to detect TB patients is crucial and should be prioritized and carried out in an active and prompt manner. TB contacts are persons who share air for prolonged periods of time with an active TB case. These include

- All prisoners who share the cell.

- Prison staff that comes in contact with a TB case
- Visitors and households

Follow-up of Released Prisoners—Prison DOTS Linkage (PDL)

- Referral tools (referral forms, Referral Directory of all BMUs in community) should be developed
- Monitoring of referrals

HIV/AIDS in Prisons

Available data show that HIV prevalence among prisoners is 6 to 50 percent higher (10 to 20 times). Drug use by prisoners and sex between men all occur in prisons in many countries.

11.2. TUBERCULOSIS CARE AND CONTROL IN REFUGEE AND DISPLACED POPULATION

The Office of the United Nations High Commissioner for Refugees (UNHCR) estimated the number of refugees, internally displaced persons (IDPs) and other people of concern to UNHCR to be more than 32 million in 2006. More than 85% of refugees originate from, and remain within, countries with high burdens of TB.

Refugees and displaced populations are at particularly high risk of developing TB. The crowded living conditions of these populations can facilitate the transmission of TB infection. Coexistent illness, particularly HIV and poor nutritional status, can weaken their immune system and make them more vulnerable to developing active TB. TB is an increasingly important cause of morbidity and mortality among refugee and displaced populations.

Given the complexity and cost of treating MDR-TB, the priority for nongovernmental organizations (NGOs) working with refugee and displaced populations is to ensure that the Stop TB Strategy using first-line TB drugs is effectively implemented. This will reduce the risk of MDR-TB and the need to use second-line TB drugs in these difficult situations.

Criteria for Implementation

The basis of an effective TB Program is the Stop TB Strategy. In refugee and displaced populations, at least the following five key elements, included in the first and major component of this strategy, must be considered a priority:

- Political commitment to TB control with sustained financing
- Case detection through quality-assured bacteriology
- Standardized treatment with supervision and patient support
- An effective drug supply and management system

- Monitoring and evaluation system, and impact measurement

Steps in Implementation

- One lead agency must be identified as taking responsibility for oversight of the TB Program. In addition, it is recommended that a TB coordinator be identified for per 50 000 population served.
- A memorandum of understanding (MoU) must be developed by the TB Program coordinator
- Staffing requirements must be estimated; job descriptions developed, staff recruited, training needs assessed and the costs and logistics of training estimated.
- Any need for patient accommodation must be determined and plans made to house a small number of very ill patients. In some settings, a larger group of patients may need to be housed in order to receive treatment because of distance to the treatment centre or other reasons.
- Existing laboratory resources – human and material – should be assessed to determine equipment needs and staff and training requirements, and be costed. A source for quality control must also be determined.
- A recording system must be established based on the Stop TB Strategy template, and the appropriate forms and registers obtained.
- Monitoring and evaluation of the Program must be ensured and regular supervisory visits should be planned, if possible with TB Program counterparts.
- A simple, locally-adapted protocol for implementation of the TB Program should be developed through consultation with the agency or agencies involved in TB care. The protocol should include steps in management of a patient with suspected TB, diagnostic algorithms, TB treatment categories and drug regimens, in line with the Stop TB Strategy. The recording and reporting system as well as that for monitoring and evaluation must also be incorporated. The protocol should also include the management of drug stocks in order to prevent TB drugs being taken and circulated freely in the community, and contingency plans for episodes of insecurity, unexpected movement of the camp or population, and repatriation or transfers to another Program. These must address the care of patients in such circumstances; arrangements should be made in advance with the anticipated Program of destination, whether in the same or another country, to ensure treatment completion. Copies of this local protocol should be available in all treatment facilities.

CHAPTER 12

TB TREATMENT IN SPECIAL CONDITIONS

12.1. PREGNANCY

A woman should be asked whether she is pregnant before she starts TB treatment. Most anti-tuberculosis drugs are safe for use in pregnancy. The exception is streptomycin, which is ototoxic to the fetus and should not be used during pregnancy. A pregnant woman should be advised that successful treatment of TB with the recommended standardized regimen is important for successful outcome of pregnancy.

12.2. BREASTFEEDING

A breastfeeding woman who has TB should receive a full course of TB treatment. Timely and properly applied chemotherapy is the best to prevent transmission of tubercle bacilli to her baby. All anti-tuberculosis drugs are compatible with breastfeeding; a woman taking them can safely continue to breastfeed. Mother and baby should stay together and the baby should be given prophylactic Isoniazid for at least 6 months. BCG vaccination of the new born should be postponed until the end of Isoniazid prophylaxis if not already vaccinated.

12.3. ORAL CONTRACEPTION

Rifampicin interacts with oral contraceptive medications with a risk of decreased protective efficacy against pregnancy. In consultation with a physician, an oral contraceptive pill containing a higher dose of estrogen (50 ug) may be taken, or another form of contraception may be used.

12.4. HIV PATIENTS ON ART

Anti-retroviral and anti-TB drugs interact reducing each other's efficacy and increasing the risk of drug toxicity; this requires adjusting the HIV or TB regimens.

12.5. TB AND DIABETES

According to a recent meta-analysis, diabetes patients have three times the risk of contracting TB as non-diabetics ^[2] The biological basis for the association between both diseases is not fully understood but studies suggest that diabetes depresses the immune response, which in turn facilitates infection with *Mycobacterium tuberculosis* and/or progression to symptomatic disease. This is corroborated by the fact that diabetes is generally diagnosed before TB develops. ^[3]

TB is more advanced at presentation in diabetics. It is more often; smear positive, present with hemoptysis, with cavitary lesions and fever. Regarding treatment; Rifampicin levels may be lower in diabetics and it raises blood glucose even in non-diabetics. Diabetics are at increased risk of drug side effects. Both of these require higher level of monitoring and dose adjustment. The WHO and IUATLD Recommendations are;

- ✓ Collaboration between TB and DM care and control initiatives
- ✓ Screening for active TB among DM people
- ✓ Screening for DM among TB patients
- ✓ Management of TB and DM co-morbidity

CHAPTER 13

HEALTH SYSTEM STRENGTHENING (HSS)- CAPACITY BUILDING

13.1. INTRODUCTION

The term ‘health systems strengthening’ refers to a process that empowers a health system to deliver effective, safe, and high-quality interventions to those who need them by improving the essential components of the system itself. Areas that require strengthening are typically the service delivery system, health workforce, health information system, systems to guarantee equitable access to health products and technologies, health financing systems, as well as leadership, governance, and accountability.

The aim of HSS in TB control Program context is to improve the overall health status of TB patients in Pakistan at the health facility and community levels. Additional aims include keeping on track the resources and money according to: goal, objective, targets and indicators. Implementation streamlining is another important aspect of HSS and a core responsibility as part of TB control Program.

13.2. WHY CAPACITY BUILDING IN NTP?

Tuberculosis is one of only several diseases for which specific control targets have been set in the Millennium Development Goals. For this efficient human resources development is vital for facilitating tuberculosis control in Pakistan and appropriate training of health Staff is an important component of this process. The purpose of trainings are to organized activity aimed imparting information and or instructions to improve the receipt’s performance or to health care provider to attain a required level of knowledge or skill.

Since the Program started, NTP is strengthening the health systems and services by improving quality in health service delivery through implementation of a Program of continuous quality improvement based on quality standards for individuals, departments and organizations against which performance will be measured. Training of health workers is an important strategy for improving health workers' productivity.

NTP for further strengthen the implementing capacity of health care providers at NTP/Provincial and district level need to be updated about the new interventions and changes occurs since last few years. The enhancement in district capacity through updated knowledge will benefit to increase the TB case detection and cure rates, expected to seek health care throughout the country.

Appropriate training of health care providers is a necessary to improve the health worker performance as well as the quality of tuberculosis control outcomes. In this context, different specific trainings for different health care provider, within the Program are distributed i-e; Doctors, Nurses, Paramedics, laboratory staff, community health workers/field staff etc. It is also mentioned here that NTP utmost tried that these trainings provided to different health care providers would be at standard /quality level. Different interventions need to scale up access to TB diagnostics and laboratories, improve the quality of supervision, and alleviate the human resource crisis by building

the capacity of health workers. The outcome of these trainings is to increase the case detection and improve treatment adherence.

13.3. HOW TO BUILD CAPACITY?

Training in TB Control Program, is an important component. Since last few years, a lot of interventions have been initiated for the Case management in all over the world as well as in Pakistan e.g. gene X-perts, change in regimen, change in definitions, change in R&R tools etc. However, for the strengthening of the NTP through Capacity Building of all cadres of health providers, NTP has already developed revised Basic Training Modules on CORE DOTS, laboratory related trainings, Multi-drug resistant TB(MDR-TB) and extensively drug resistant(XDR-TB)cases ,TB/HIV, Infection Control, revised R&R Tools are utilizing as reporting and recording tool etc for the training purpose for different categories Health Care Providers etc .Also refresher course has been conducted for these health care providers, at least two years after basic trainings. It is important to evaluate the contribution of training to improving health workers' productivity and the quality of TB Control Program. Such evaluation can be occurring at three levels: (a) During training, through feedback from participants, quality of written and practical training-related assignments undertaken by participants, and pre-test/post-test evaluations; (b) site visits by trainers, to observe participants in clinical and field conditions; (c) evaluation of tuberculosis Program outcomes, with particular attention to improvements in case detection rates and cure rates. Evaluating the quality of trainings may be assessed during the training courses. These trainings are also monitor and supervised by senior level technical Staff.

These standardize training curriculum for basic & refresher training on different component of TB Control Program, for health care providers are available in the Program, along wide variations in training duration, e-g;

- The duration of Basic/Refresher Core DOTS Training is 04 days for doctors, 02 days for Paramedics and 02 days for Managers.
- The duration of Management of Childhood TB Trainings for doctors and Paramedics is of 02 days.
- The duration of TB/HIV trainings for doctors is 2days, for field officers are for 2 days
- Intervention Based Trainings on X-pert, MDR and Infection control

13.4. ORGANIZING & MANAGING TRAININGS

All trainings are conducted according to the given targets and National Training policy. Arrangements are made for specific training courses of each staff category. It is very important to train various categories i-e; managers, doctors, paramedics, lab, related staff, field staff of different components of TB Control Program, at the national, provincial and district levels. It is also important that the activities of TB Control cannot be start in a particular facility until and unless, all the relevant trainings course have been completed for each type of staff in that facility.

The trainings of health care providers will be arranged/conducted by of PTP's. An approved detailed National Training Plan (including targets, tentative list of participants with designation, venue, dates, facilitators etc.) is submitted to all PTP's for implementation of activities at Provincial as well as

District Level. The advance for training/budget breakup is including TA/DA, refreshment, stationary and administrative support etc. The facilitators are nominated by Provinces, who are already certified master trainers. He or she must have attended different basic trainings on Core DOTS, Supervisory Modules; Laboratory related trainings, trained in TB/HIV co-infection, HDL/Childhood TB Management and basic training on MDR etc. The laboratory personnel would be trained at the Provincial Reference Laboratory or National Reference Laboratory. Special approval may be granted for special case from competent authority. After receiving training plan from Provinces, NTP finance unit with the support of internal audit unit release and transfer of funds/advances of trainings, to the official accounts of PTP's. The staff at National and Provinces are trained in audit and financial management for the strengthening of the Program.

After the completion of trainings, PTP's are responsible to submit the original SOE's (with all required documents) to NTP through proper channel where these SOE's are scrutinized by PIU, finance and internal audit wing for the final settlement.

SECTION-III

DRUG RESISTANT TUBERCULOSIS

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CHAPTER 14

DRUG RESISTANT TB

Drug resistance tuberculosis (DR-TB) is caused by mycobacterium organisms that are resistant to a first-line or second-line anti-TB drug. The term DR-TB is used as it covers, in addition to DR-TB, other different types of drug resistant TB are;

- **Mono-resistance:** resistance to one anti-TB drug.
- **Poly-resistance:** resistance to more than one first line anti-TB drug (excluding both Isoniazid (H) and Rifampicin (R) at a time).
- **Multi-drug-resistance (MDR):** resistance to both Isoniazid (H) and Rifampicin (R) with or without resistance to any other drug.
- **Extensive drug-resistance (XDR):** resistance to any Fluoroquinolone and at least one of the three injectable second-line drugs (Kanamycin, Amikacin or Capreomycin) in addition to multidrug resistance.

Pakistan ranks 4th among 27 high Drug Resistant (DR) TB burden countries in the world. The recent DR survey in Pakistan has reported 3.7% in new TB cases and 18.1% resistance in re-treatment cases. WHO has estimated an annual incidence of about 13,000 DR-TB cases in Pakistan in 2013 (WHO report 2014). Since the Beijing's call for action in April 2009, the National TB Program (NTP) Pakistan has shown its commitment to address DR-TB through a structured and comprehensive approach, which includes developing policies, strategies, guidelines and phased expansion of implementation activities.

The Program's target is to enhance the capacity of public and private sectors to detect and manage 80% of the estimated smear positive DR-TB incident cases by year 2015. The Program is strengthening sixty-six (66) X-pert sites, six (6) DST Laboratories, sixteen (16) Culture laboratories and thirty (30) PMDT Treatment Sites at teaching and specialized hospitals (both public and private sector) across the country.

14.1. DIAGNOSTIC APPROACH TO DR-TB

The Introduction of GeneX-pert has facilitated diagnoses of Rifampicin resistant and National policy recommendation has been formulated based on

- Difference in Prevalence of DR in retreatment versus new TB cases
- Potential high risk group for DR among NEW patients
- Need for early diagnosis of TB in vulnerable population

Considerations have also been taken into account concerning operational challenges in referral and specimen transportation, turnaround time (TAT), infrastructure constraints and resource implication.

SCREENING OF DRTB PRESUMPTIVE CASES:

The use of X-pert/MTB Rif has been recommended as a first diagnostic testing for screening to the following high risk groups (DR-TB presumptive cases)

A. ALL RETREATMENT TB CASES: All TB cases (AFB B+ve or clinically diagnosed) with history of previous ATT should be tested for X-pert at month zero of enrolment. This includes:

- Treatment Failure Cat-I
- Treatment Failure Cat-II
- Relapse after Cat-I
- Relapse after Cat-II
- Treatment after loss to follow up Cat-1
- Treatment after loss to follow up Cat-II
- Other Retreatment

B. SYMPTOMATIC CONTACTS OF DR-TB PATIENT: All household and workplace symptomatic contacts of DR-TB patients should be screened for drug resistance. Specimen from these individuals should be processed for AFB smear and then the specimen is referred for X-pert MTB/Rif assay irrespective of smear results.

C. TB PATIENTS UNDER TREATMENT WHO FAIL TO CONVERT AT THE END OF INTENSIVE PHASE

- SS+ve patient on Cat-1 who fail to convert at the end of month #2 of treatment.
- SS+ve patient on Cat- II who fail to convert at the end of 3 months.
- SS-ve Patient who is reported AFB smear positive at the end of intensive phase

Comprehensive First and second line DST: All patient who are reported Rifampicin resistant on X-pert/MTB Rif assay should be referred to MDR treatment site and specimen should be referred to quality assured DST laboratory for comprehensive first and second line DST before start of treatment.

If patient is reported Rifampicin sensitive on X-pert MTB/Rif assay but is clinically considered at high risk of MDR (e.g. Cat-II-failure), patient may be referred for phenotypic drug susceptibility testing as small number of Rifampicin resistant are not detected by X-pert MTB/Rif assay

14.2. DURATION OF TREATMENT

The recommended duration of treatment is guided by culture conversion for a minimum of 18 months after culture conversion. The treatment is divided into Intensive and Continuation phases.

Extension of therapy to 24 months may be indicated in chronic cases with extensive pulmonary damage.

14.3. PROCESS OF MANAGEMENT

14.3.1. IDENTIFICATION OF MDR-TB PRESUMPTIVE CASES

Cat-II failure and DR-TB contacts are TB presumptive cases. The Doctor at the TB clinic will assess patient's DR-TB risk on the basis of: Record review and in-depth Interview with the patient. On suspicion of DR-TB the patient will be given health education and referred to nearest PMDT Site (hospital for diagnosis and treatment). In addition, the groups mentioned in the section above are also to be considered.

14.3.2. HOSPITAL BASED CARE

The newly diagnosed DR-TB patient may be hospitalized (at PMDT site) for some time to make clinical assessment, see initial reaction to the prescribed second line drugs and to make satisfactory arrangements for community-based management of DR-TB patient.

14.3.3. AMBULATORY BASED CARE

The DR-TB Patients are recommended for ambulatory based care if:

- a. Patient's clinical condition deem suitable,
- b. Treatment Supporter is identified for 'DOT'
- c. An accessible and functioning DR-TB Clinic is identified for community-based DR-TB care.
- d. No adverse reaction to second line drugs observed in first 15 days, and

All DR-TB patients under ambulatory management, visit their treatment hospitals for monthly follow-up assessments, including clinical monitoring, drug compliance and sputum cultures.

14.3.4. TREATMENT SELECTION OF DR-TB CASES

In principle the following criteria (table below) can be used as guiding principles in treatment selection which is in line with the National Guidelines of DR-TB management, WHO and other well know International Guidelines for DR-TB (For more information on treatment selection, please refer to the National Guidelines for DR-TB management):

DR-TB Enrolment

The following groups are **eligible to be enrolled** on DR-TB treatment:

- a- Patients detected as Rifampicin resistant on GeneX-pert.
- b- Patients who have been confirmed to have DR-TB by DST

- c- Patients with strong suspicion (high likelihood) of DR-TB (in absence of Gene-X-pert, the patient might be enrolled on treatment while waiting for DST results).

Table 11: Treatment Selection (DR-TB)

Patient previous SLD history and DST	Treatment Selection
Patient did not use SLD before (or not found to be resistant to SLD)	8 Am-Lfx-Eto-Cs-Z+ B6 / 12 Lfx-Eto-Cs-Z+ B6
Patient received FQ previously (or found to be resistant to FQ)	8 Am-Lfx-Eto-Cs-PAS-Z+ B6 /16 Lfx-Eto-Cs-PAS-Z+B6
Patient received Am or Km previously (or found to be resistant to Am or Km)	8 Cm-Lfx-Eto-Cs-Z+B6 /16 Lfx-Eto-Cs-Z+B6

Group-1	First-line oral anti-tuberculosis drugs which include Isoniazid (H), Rifampicin (R), Ethambutol (E), and Pyrazinamide (Z)
Group-2	Injectable anti-tuberculosis drugs which include Streptomycin (S), Kanamycin (Km), Amikacin (Am) and Capreomycin (Cm)
Group-3	Fluoroquinolones which include Ofloxacin (Ofx), Levofloxacin (Lfx), and Moxifloxacin (Mfx).
Group-4	Oral bacteriostatic second-line anti-tuberculosis drugs such as Ethionamide (Eto), Prothionamide (Pto), Cycloserine (Cs), Terizidone (Trd), and P-aminosalicylic acid (PAS)
Group-5	Anti-tuberculosis drugs with unclear efficacy (not recommended by WHO for routine use in MDR-TB patients). These may include Clofazimine (Cfz), Amoxicillin/Clavulanate (Amx/Clv), Clarithromycin (Clr), Linezolid (Lzd), Thioacetazone(Thz), Imipenem/Cilastatin(Imp/Cln),and High Dose INH.

14.3.5. SOCIAL SUPPORT PACKAGE

TB patient compliance to treatment both in sensitive and drug-resistant TB is a known problem. In the case of treatment for DR-TB the patient has to take the medicines for two years which is a significant challenge, not only for the patient but also for the care givers/families who are supporting him/her in this treatment. Keeping in view the above stated factors, and to enhance the compliance of patient to treatment, the NTP is offering social support to DR-TB patients as well as their treatment supporters with a “food basket coupon” and “travel reimbursement” to the patient on his/her monthly follow-up visit to the hospital.

CHAPTER 15

TUBERCULOSIS INFECTION CONTROL

15.1. INTRODUCTION

Rapid detection of pulmonary TB patients should be the priority for every health facility, so that those patients can be treated before spreading the infection. Thus, fast detection of the most infectious cases and proper treatment are two of the most important ways to prevent TB transmission.

Smear-positive pulmonary TB patients are the most infectious cases because they spray tubercle bacilli into the air whenever they cough or sneeze. Contacts of smear-positive cases may become infected when they breathe in tubercle bacilli. The longer sputum smear positive cases are present in the home and community before beginning treatment, the greater the chances that they will infect others.

Promptly identifying people who cough, separating them from other patients to the extent possible, asking patients to cover their mouth and nose when coughing or sneezing (cough hygiene), and minimizing the amount of time that patients are in the health facility are all ways to decrease the possibility of transmission of TB and other airborne infections in the facility.

Another way to prevent TB transmission is to bring fresh air into areas of the health facility where infectious TB patients and TB presumptive cases cough or sneeze while waiting, seeing a health worker or walking from one area to another. Good ventilation dilutes and exchanges the room air with fresh air, thereby reducing the number of particles remaining in the air and reducing the risk of another person becoming infected with TB in the facility.

Poor hand washing practices allow transmission of other infections. It is therefore vital that health workers stay alert of the possible routes that infections can be transmitted and take very seriously the procedures and precautions that prevent the spread of illness.

15.2. PRINCIPLES OF TB-INFECTION CONTROL

15.2.1. ADMINISTRATIVE CONTROL

To reduce the risk of exposure to TB presumptive cases by ; a) assigning responsibilities to implement infection control plan; b) introduce patient management practices; c) premises cleanliness; d) training & testing of staff; e) usage of appropriate signage's; and f) coordination between departments.

15.2.2. ENVIRONMENT (AIRBORNE) CONTROL

- Primary control: by controlling source of infection by using air mixing, dilution & removing contaminated air by using general ventilation.
- Secondary control: by controlling the airflow to prevent contamination of air and cleaning the air by using high efficiency particulate (Hepa) filtration & Ultraviolet germicidal irradiations (UVGI'S)

15.2.3. USE OF PERSONAL PROTECTIVE EQUIPMENT (PPE)

Use of particulate respirator (N95 masks) for HCWs when caring for patients suspected or known to have infectious TB, in particular drug-resistant TB patients.

NOTE: Masks are NOT a substitute for administrative or environmental controls. Masks will improve personal protection when administrative & environmental controls are functioning optimally.

15.3. TB INFECTION CONTROL IN HEALTHCARE, COMMUNITY & CONGREGATE SETTINGS

15.3.1. TB IC IN HEALTH CARE FACILITY

Broad Areas of Infection Control suggested to be covered in TB-IC at health facility must include implementation following the process described in the table below:

Table 12: Infection control in health facility

S. No	Area of Service	Managerial	Administrative	Environmental	Personal Protection
1	Outpatient Area	TB IC focal person	Triage & Screening	Natural Ventilation	Surgical Masks & N-95 provision to patients, attendants and Health Care Workers
		Tb Risk (re)Assessment	Fast Tracking	Mixed Mode Ventilation	
		Development of TB IC Plan	Separation Rooms		
		ACSM Plan	Minimize Time Spent	Safe Waste Disposal	
		Monitoring & Evaluation	Cough Etiquettes		
		Staff Training	Periodic TB Staff Screening	UVGI & ACH maintenance	
2	Sputum Microscopy Laboratory	Medical Technologist Responsible	Separate (open space) Sputum Collection Area	Natural Ventilation	N-95 or FFP2 fit testing when performing DST
		Bio-Risk Assessment	Minimize Time Diagnosis	Mixed Mode Ventilation	
		Bio safety plan with training	Periodic TB Staff Screening		Safe Waste Disposal
		Monitoring & Evaluation			

3	Sputum Collection & Smearing Centre	TB IC Risk (re) Assessment	Well ventilated waiting area	Natural Ventilation	N-95 provision
		TB IC Plan with Training	Cough Etiquettes Face Masks		
		ACSM Plan with Training	Minimize Time Diagnosis	Safe Waste Disposal	
		Monitoring & Evaluation	Periodic TB Staff Screening		
4	Radiography	Radiographer Responsible	MDR patients priority	Natural Ventilation	Masks and N-95 provision to patients and staff
		Policies for handling suspects	Fast Tracking		
		Development of SOPs	Proper Spacing of patients	Mixed Mode Ventilation	
5	MDR-TB Ward	TB IC focal person	Separation and isolation rooms	Natural Ventilation	N-95 or FFP2 staff
		TB IC Risk (re) Assessment	Visitors Restriction	Mixed Mode Ventilation	N-95 or FFP2 visitors when indoors
			Cough Etiquettes, Face Masks		
		Monitoring & Evaluation	Minimize Time Spent	UVGI & ACH maintainace	
		TB IC Plan with Training	Periodic TB Staff Screening	Safe Waste Disposal	Fit Testing Staff

6	XDR-TB Ward	TB IC focal person	Separation and isolation rooms	Natural & Mixed Mode Ventilation	N-95 or FFP2 staff
		TB IC Risk (re) Assessment	Visitors Restriction	UVGI & ACH maintenance	N-95 or FFP2 visitors when indoors
			Cough Etiquettes, Face Masks		
		Monitoring & Evaluation	Minimize Time Spent	Safe Waste Disposal	Fit Testing Staff
		TB IC Plan with Training	Periodic TB Staff Screening		
	Responsibility	Hospital Administrator	Hospital Infection Control Team	Hospital Management	Hospital Management/NTP for Fit testing

15.3.2. TB IC in community (households)

Reduction of transmission of TB in particular MDR-TB in households is necessary because the household members are at high risk of becoming infected and consequently developing TB. The primary objective for TB-IC measures are carried out in household settings is to reduce the likelihood of TB transmission to others in the household.

15.3.3. TB IC in congregate settings

TB-IC measures need to be implemented in congregate settings (e.g. Prison cells: barracks: refugee camps, dormitories, nursing homes, and settings which provide services for PLHIV) where people have a higher risk of TB transmission due to confined spaces. All sites where people with high burden of TB are gathered needs incorporation of TB-IC measures to reduce the risk of transmission.

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TB and HIV

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CHAPTER 16

TB-HIV CO INFECTION

16.1. INTRODUCTION

HIV is the strongest risk factor for developing tuberculosis (TB) disease in those with latent or new *Mycobacterium tuberculosis* infection[15]. The risk of developing TB is between 20 and 37 times greater in people living with HIV than among those who do not have HIV infection. TB is responsible for more than a quarter of deaths in people living with HIV. In response to the dual epidemics of HIV and TB, the World Health Organization (WHO) has recommended 12 collaborative TB/HIV activities as part of core HIV and TB prevention, care and treatment services.

Pakistan is a low HIV burden country. The prevalence of HIV infection in general population is less than 0.1%. The existing sentinel surveillance system has indicated that the prevalence of HIV infection among TB patients was 0.4 percent in 2013.

Although Pakistan is a low HIV prevalence country, there are 86,467 people living with HIV (PLHIV) [16] and are at high risk of being affected with TB. The NTP Pakistan working together with AIDS control Program has established National TB/HIV Collaborating Board, and provincial level TB/HIV coordination committees which have been constituted in the four provinces. There are currently 16 sentinel sites (expansion in process) which focus on the surveillance of HIV infection in TB patients. These sites are health facilities that provide TB diagnosis and treatment services in which diagnosed TB patients are offered HIV counselling, screening and referral services.

16.2. REDUCE THE BURDEN OF TB IN PEOPLE LIVING WITH HIV AND INITIATE EARLY ANTIRETROVIRAL THERAPY (THE FOUR I'S FOR HIV/TB)

Care providers for tuberculosis and HIV patients at all levels must be well versed with both conditions. The philosophy of care must be “two diseases, one patient, and one system”^[17]. The four *I's* are considered as very important in management of TB/HIV cases. These include (a) intensive case finding, (b) Infection control, (c) INH prophylaxis and (d) Integrated case management.

16.3. INTENSIFY TB CASE-FINDING AND ENSURE HIGH-QUALITY ANTI-TUBERCULOSIS TREATMENT

Screening for TB: All people living with HIV, wherever they receive care, should be regularly screened for TB using a clinical algorithm at every visit to a health facility or contact with a health worker (see chapter on TB Case finding and diagnosis). Screening for TB is important, regardless of whether they have received or are receiving IPT or ART. It is recommended that in most settings, the symptom-based rule should be implemented.

Adults and adolescents living with HIV: Screened for TB with a clinical algorithm for any one of the symptoms i.e. current cough, fever, weight loss or night sweats.

- Those who report may have active TB and should be evaluated for TB (see chapter on Case finding and TB diagnosis) and other diseases
- Those who do not report any one of the symptoms are unlikely to have active TB and should be offered IPT.

Children living with HIV: should be evaluated for symptoms of poor weight gain, fever, current cough or contact history with a TB case.

- Those who have any one of these may have TB and should be evaluated for TB (see chapter on Case finding and TB diagnosis) and other conditions. If the evaluation shows no TB, they should be offered IPT regardless of their age
- Who do not have these symptoms are unlikely to have active TB

16.4. INITIATE TB PREVENTION WITH ISONIAZID PREVENTIVE THERAPY

Adults and adolescents living with HIV: Adults and adolescents living with HIV who have an unknown or positive TST status and who are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals irrespective of the degree of immune suppression, and also to those on ART, those who have previously been treated for TB and pregnant women.

Children living with HIV: who are;

- More than 12 months of age and who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services.
- Less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease.
- All children living with HIV who have successfully completed treatment for TB disease should receive INH for an additional six months

16.5. REDUCE THE BURDEN OF HIV IN PATIENTS WITH PRESUMPTIVE AND DIAGNOSED TB

16.5.1. PROVIDE HIV TESTING AND COUNSELLING TO PATIENTS WITH PRESUMPTIVE AND DIAGNOSED TB

Establish HIV testing and counselling facilities or referral mechanism between Tuberculosis BMU and facilities offering testing facilities to patients with presumptive and diagnosed TB in district with documented high epidemics.

16.5.2. INTRODUCE HIV PREVENTION INTERVENTIONS FOR PATIENTS WITH PRESUMPTIVE AND DIAGNOSED TB

All personnel working with presumptive and confirmed TB cases, people living with HIV and people who use drugs should be able to assess risk factors for HIV infection and transmission and should provide comprehensive information and services to their clients to minimize their risks.

16.5.3. PROVIDE CO-TRIMOXAZOLE PREVENTIVE THERAPY FOR TB PATIENTS LIVING WITH HIV

Routine co-trimoxazole preventive therapy should be administered in all HIV-infected patients with active TB disease regardless of CD4 counts.

16.5.4. ENSURE HIV PREVENTION INTERVENTIONS, TREATMENT AND CARE FOR TB PATIENTS LIVING WITH HIV

All people living with HIV who are diagnosed with TB should receive integrated services for prevention, diagnosis, treatment and care of TB and HIV.

16.6. TB TREATMENT

TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of Rifampicin treatment regimen. The optimal dosing frequency is daily during the intensive and continuation phases. The details of TB treatment is described in the relevant chapter above.

16.7. HIV TESTING AND COUNSELLING (HTC)[18]

HIV testing and counseling (HTC), must adhere to the five Cs—Consent, Confidentiality, Counseling, Correct test results and linkage to Care. Scaling-up of provider initiated testing and counseling (PITC) should be considered in TB clinic located in district with HIV epidemics.

To improve the quality of service delivery and the acceptability and uptake of HTC, for many settings WHO recommends the use of rapid diagnostic tests (RDTs) rather than conventional laboratory based diagnostics such as enzyme immunoassay (EIA). RDTs allow quicker provision of test results and post-test counseling. Most RDTs do not require venipuncture specimen collection, but instead can be performed with simple finger-stick collection procedures.

SECTION-V

MONITORING AND EVALUATION

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CHAPTER 17

TB CONTROL: MONITORING AND EVALUATION

17.1. INTRODUCTION

The assessment of efficiency and effectiveness of TB control Program implementation requires a structured and well established monitoring & evaluation system in the country. The Program performance will be monitored against specified set of indicators which provides information on inputs, performance, outcome and impact achieved by the TB control Program at district, provincial and national level in a specified quarter and for a complete year.

17.2. M&E ARRANGMENTS

The NTP/PTPs has an efficient Monitoring and Evaluation (M&E) system in place, which is the backbone to maintain the quality of TB services in the country. The NTP/PTPs has developed structured approach and tools for M&E which are based on bottom-up approach i.e. community to facility up to the national level. TB care facilities in the district, which is the basic implementation unit, has been integrated into the routine district health care system. District TB coordinator (DTC), assigned from public health sector is responsible to manage TB care activities in district.

Provincial M&E units facilitated by NTP are overall responsible for planning and implementation of monitoring and surveillance activities. The monitoring carried out by the Provincial Technical Officers (PTOs), National Program Officers (NPOs), M&E officers of specific interventions (PPP, MDR, lab etc.). The monitoring carried by NTP is through National Technical Officer (NTO), supported by M&E specialist and objective coordinators. There are also quality assurance systems for laboratory function which are established at the level of districts carried by District Laboratory Supervisor (DLS), Provincial Reference Laboratory (PRL) and National Reference Laboratory (NRL).

17.3. PLANNING AND REPORTING TIMELINES& TOOLS

There is a structured process and responsibilities to carry out M&E activities as described in the table below:

TABLE 13: M&E SCHEDULE AND RESPONSIBILITIES

Activity	Timeline	Responsibility	Remarks
Submission of activity/M&E plan by relevant staff for next month to M&E Unit NTP	25 th of preceding month	Project Implementation Unit	Soft copies only
Submission of activity plans of all implementing partners for next month to focal person PTPs	25 th of preceding month	All implementing partners	Soft copies only
Review and endorsement of plans of all implementing partners by PTP	26 th of preceding month	Focal person PTP	Soft copies only
Communication of activities of all SRs to all NPOs/M&E Officers in the province for incorporation in their M&E plans	26 th of preceding month	All PTOs	Soft copies only
Submission of activity plans of principal recipients and their implementing partners for next month to M&E Unit NTP	27 th of preceding month	Coordinator NTP	Soft copies only
Submission of activity/M&E plan of all NPOs/M&E officers for next month to PTO/PTP Manager	27 th of preceding month	All NPOs/M&E officers	Soft copies only
Communication of M&E visit plans of next month to PTOs/PTP Managers	27 th of preceding month	All NPOs/M&E officers	Soft copies only
Finalization and submission of activity plans of PTO/NPOs/M&E Officers for next month to M&E Unit NTP	29 th of preceding month	ALL PTOs	Soft copies only
Finalization and circulation of monthly consolidated M&E plan for next month to all concerned.	Last working day of preceding month	M&E Unit NTP	Soft copies only
Submission of visit reports for feedback through email to; <ul style="list-style-type: none"> PTO (for NPOs/ M&E Officers) M&E Unit NTP 	Up to 10 th of next month	All concerned	Soft copies only
Communication of feedback from PTO and M&E Unit NTP	Up to 15 th of next month	PTO/M&E Unit NTP	Soft copies only

17.4. DATA COLLECTION AND REPORTING FORMS AND TOOLS

The Program has developed standardized recording and reporting tools in line with WHO guidelines for Core DOTS. These tools are revised conferring to WHO guidelines. The following table is a summary of the list forms that will be used strictly for core TB DOTS and MDR monitoring and evaluation. In addition, ERNS is in place in few pilot districts for core DOTS and MDR Electronic Nominal Registration System (MDR ENRS) at all PMDT sites.

TABLE 14: LIST OF COMMONLY USED TOOLS

CORE DOTS	MDR-TB
<ul style="list-style-type: none"> ▪ TB 01 Facility Based Patient Treatment Card ▪ TB 02 Patient Identity Card ▪ TB 03 Patient Registration Register ▪ TB 04 Laboratory Register ▪ TB 05 Lab Request Form for biological specimen examination ▪ TB 06 Lab Culture Request Form ▪ TB 07 Quarterly Registration Reporting Form ▪ TB 08 Quarterly Sputum Conversion Reporting Form ▪ TB 09 Quarterly Treatment Outcome Form ▪ TB 10 Referral form (Pre & Post registration) /referral register ▪ Contact register 	<ul style="list-style-type: none"> ▪ DR-TB 00 History and Physical Examination Form ▪ DR-TB 01 Patients Treatment Card ▪ DR-TB 02 Patient's Identity Card ▪ DR-TB 03 ENRS Patients Register with Pharmacia - vigilance ▪ DR-TB 04 DR-TB Laboratory Register for Referring Sites ▪ DR-TB 05 Request form for Smear, X-pert, Culture, DST ▪ DR-TB 06 Detection Indicator ▪ DR-TB 07 Enrolment Indicator ▪ DR-TB 08 Interim Result Indicator ▪ DR-TB 09 Annual Outcome Indicator ▪ DR-TB 10 Referral Form for DR-TB presumptive case Diagnostic and Management ▪ DR-TB 11 Status of Second Line Drugs Report ▪ DR-TB 12 Quarterly Request for SLD from Warehouse ▪ DR-TB 13 Questionnaires to Record ADRs ▪ DR-TB 14 SLD Prescription Form ▪ DR-TB 15 Treatment Support Card

17.5. DATA VALIDATION

The data is comprehensively verified during the quarterly surveillance meeting. Quarterly surveillance meetings are held at district, provincial and national levels. The data is consolidated for about 1500 reporting BMUs and TB care facilities from public and private sector of 142 districts in all provinces/regions, processed at NTP and dissemination to all concerned quarters, nationally and internationally. The arrangements include; Intra District Quarterly Surveillance Meetings, Inter District Meetings and Inter Provincial Meetings.

NTP also carries out national and international reviews and PPP is also part of these reviews. The data is also being verified during these reviews. In addition, M&E of DR-TB is a vital component of NTP which is done mainly for the PMDT sites in the country.

The monitoring of public-private mix component of TB control Program at district level is the responsibility of District TB Coordinator.

17.6. M&E INDICATORS

The Program has defined indicators to cover both GF requirement and programmatic needs. The indicators are in line with WHO and global fund guideline. The data is mainly reported on a) Core DOTS; b) Childhood TB; c) PPP; d) DR-TB; e) TB/HIV; and f) Laboratory indicators.

17.7. SURVEILLANCE:

Surveillance is integrated in the M&E plan based on M&E indicators to measure performance. At the district level Basic Management Unit (BMUs) at primary and hospital level are the registration (TB03 register) and quarterly reporting units (case notification TB07 and treatment outcomes TB09). The reports are consolidated from each of the BMU first at district level and then at provincial and national level. Paper based TB data is generated and recoded on structured formats from TB care facilities. Data is communicated from BMU to national level on both hard and soft version. NTP has also introduced e-surveillance online TB data collection system titled as “MIS-DOTS” in 2012 and gradually expanding in all 142 districts by 2014. There are more than one version of this software and need to be standardized all over the country. TB data is compiled, validated and analyzed on M&E indicators during quarterly surveillance meetings, scheduled at district, provincial and national levels following conclusion of every quarter. Internal and international Program reviews and third part evaluations are also conducted.

The NTP M&E units monitor progress in two areas; *first*, and most immediate, is performance data monitoring. Data is regularly collected and reported each quarter to show performance at each level towards achieving the targets on indicators. *Second*, the M&E unit monitor progress on the activities scheduled in the Annual Work-plans using the M&E Field Visit Tools (see National M&E Module, NTP M&E plan and specifically developed checklists).

SECTION-VI

PHARMACEUTICAL AND HEALTH PRODUCT MANAGEMENT (PHPM)

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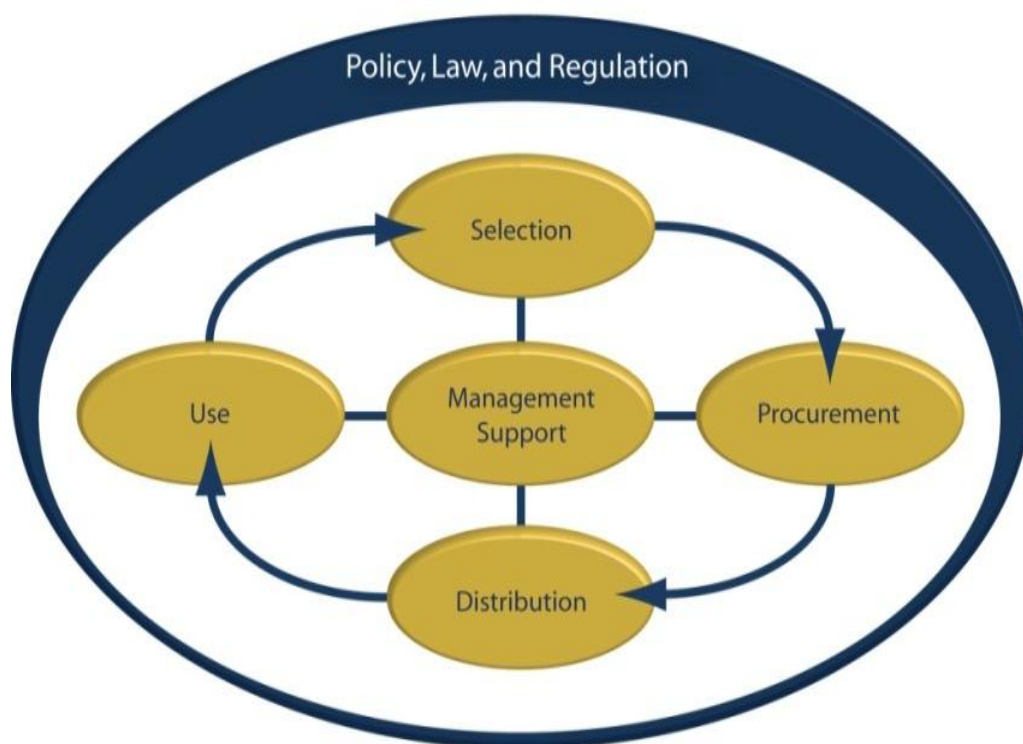
CHAPTER 18

PHARMACEUTICAL AND HEALTH PRODUCT MANAGEMENT

18.1. INTRODUCTION

The Pharmaceuticals and Health Products are an essential component of TB care & prevention. ATT are included in the National Essential Medicines List (NEML) and provincial MSDS/EHSP of Pakistan as well as World Health Organization EML. The NTP recommends that individuals with the disease receive adequate and timely diagnosis and treatment through a well-functioning supply chain management. These guidelines are written to set out a framework for such a pharmaceutical & health products management system which ensures that TB patients get uninterrupted access to recommended anti-TB treatment (ATT) medicines and lab supplies of good quality and use these rationally. The details have been described in the relevant section. Symptom based screening approach to child contact management is presented below which has been adapted from WHO guidelines.

Figure 3: PHPM Cycle



A TB PHPM management system involves four basic functions: *selection*, *procurement*, *distribution*, and *use*. Each of the four basic functions of the cycle is described below in detail.

18.2. SELECTION OF PRODUCT

Selection is the process of choosing the most appropriate PHPs for TB Programs from a limited list of essential medicines and WHO TB Tools for labs. The selection criteria are based on factors such as disease prevalence, clinical evidence, appropriate treatment regimens, availability, costs, quality, efficacy, safety, simplicity of stock management, and adherence of TB patients to the treatment protocol. The appropriate regimen should be according to National and International guidelines and must fall in essential medicine list / formulary.

18.3. PROCUREMENT OF PRODUCT

Procurement is the process of obtaining PHPs through a competitive, transparent and accountable process of purchase. Careful procurement planning is required at all levels for optimal use of available resources in procuring good-quality products at the most economic prices. National TB Control Program procures pharmaceuticals and health products from international market (donor funds) as well as from local market through public procurement.

International procurement: WHO recommends that national TB Programs select ATT medicines & lab supplies from the WHO Model List of Essential Medicines [19] & WHO TB Tool (all of them are listed by generic name or international nonproprietary name). Such selection ensures that only PHPs with scientific evidence for efficacy and safety are listed. Additionally, the selection criteria are extended to the PHPs of manufacturers listed under the WHO Certification Scheme. (WHO Prequalified Manufacturers).

National procurement: Selection of all essential medicines and lab supplies to be procured is authorized by the Departmental Purchase Committee, which prepares the list of products to be purchased based on (National Guidelines, EML & Lab items details) and the Rate Contract List. For quality assurance of Pharmaceutical Products, it is mandatory that only those manufacturers and products are eligible to participate in bidding who have successfully undergone the process of Bioavailability / Bioequivalence (BA/BE) studies, from WHO Pre-qualified BA/BE labs across the globe or labs those are authorized by Drug Regulatory Authority of Pakistan to conduct BA/BE studies.

The government hospitals and districts shall adopt same criteria while procuring the ATT medicine.

18.4. REGISTRATION

As mentioned earlier, any PHP to be procured for use in Pakistan has to be registered with the DRAP by the potential suppliers for in country procurement. However, a waiver in registration need to be sought in case of donations (in kind) from quality assured sources abroad.

18.5. QUANTIFICATION

For quantification of ATT medicine, the *morbidity / consumption-based method is followed*. This method forecasts the future needs based on the number of expected TB and symptomatic respiratory cases, consumptions trends, available stock and stock in pipeline. The quantities of medicines to be procured are to be calculated according to 'known needs' plus a buffer / reserve

stock to cover unexpected delays in resupply. NTP recommends 100% buffer stock to be available in country for its annual needs. The distribution of buffer stock will be as; 50% national level, 25% provincial and 25% at district level.

While for the procurement of lab supplies national TB morbidity based forecasting method is followed.

18.6. QUALITY ASSURANCE

The NTP and provincial Programs for control of TB should procure PHPs that meet the quality standards for manufacturers whose products and manufacturing sites are prequalified by the UN prequalification Program for international procurements and should be tested for BA/BE for local procurements.

18.7. DISTRIBUTION

The process of *distribution* can be categorized into major groupings of activities—the overall system design, including the different organizational levels; the supporting information systems (electronic and hard copy); inventory management; and both the transport and storage operations. Their collective objective is to provide a cost-effective distribution system that ensures a continuous supply of PHPs in a usable condition is made available to TB patients' and diagnostics centers.

18.8. STORAGE

Currently, medicines are mainly stored at National, provincial and district warehouses. At all these levels the Program has well established warehousing facilities those meet the requirements of Good warehousing practices (GWP) and has sufficient storage capacity to cater the buffer stocks across the supply chain.

Good practice in the management of these storage facilities should ensure that the following protocols are fully addressed—

- Infrastructure—handling equipment, racking, shelving, movement of items, refrigeration units, power supply, pallets
- Facility layout—zoning , materials flow, appropriate working environment
- Receipt & Issuance ----- Quarantine area, Physical Inspection/Count & Inventory Control
- Electronic Recording & Reporting System-- TB DMIS and WMS across the supply chain
- Environmental conditions—temperature/moisture control, dust control, control on direct sunlight, pest control
- Human resources—personnel, training, job descriptions, communications

- Security—recording systems, controlled access, building integrity, auditing procedures
- Support systems—electronic, manual, mixed, forms, instructions, reporting
- Good working practice— FEFO & FIFO stock rotation, disposals, documented procedures
- The system of Quality Assurance across the supply chain

Details on the specific requirements and instructions on Good Warehousing Practices as it relates to the TB Program can be viewed in the Operational Manuals.

18.9. TRANSPORT

The movement of medicines from the initial port of entry to the national storage operations, through the provinces, to the districts, and on to the facilities requires detailed oversight.

NTP recommends safe, timely and quality assured delivery of PHPs from National level to PTPs and from Provincial TB Programs to districts and onward supplies to health facilities.

18.10. RATIONAL USE OF ATT MEDICINES

The concept of rational use in the context of pharmaceutical management is that patients receive correct medication and adhere to the treatment protocol. For details please refer to Drug Management Guidelines and Dispensing Manuals.

18.11. MANAGEMENT SUPPORT

Management support is located at the center of the PHPM cycle and is cross cutting activity. The roles of this core function are to review the current practice of the four components of the cycle (selection, procurement, distribution/storage, and use) comprehensively and to identify the weaknesses and invest necessary resources to overcome those weaknesses. From National TB Control Program to Provincial TB Control Programs till district health authorities, each management cadre is responsible for its role in supporting the Pharmaceutical and Health Product Management.

18.12. PHARMACOVIGILANCE

The pharmacovigilance system for ATT medicines should be designed to detect, assess, understand, and prevent adverse effects, particularly the long-term and short-term side effects of medicines. The aims of pharmacovigilance are to enhance patient care and patient safety in relation to the use of medicines, thus encouraging safer and more effective use of medicines and a resolution of the sometimes apparently conflicting interests of public health and individual patient welfare. A comprehensive National guideline on Pharmacovigilance is in development phase and will encompass the subject in detail.

18.13. DISPOSAL OF EXPIRIES AND WASTE

Once past their expiry date, ATT medicines become less efficacious and may develop a different adverse drug reaction profile. A number of methods exist for safe disposal of expired and wasted ATT medicines[20]. These methods involve minimal risks to public health and the environment. The main disposal methods suitable for ATT medicines are as follows—

- Return to donor or manufacturer—wherever practical, the possibility of returning unusable medicines for safe disposal by the manufacturer should be explored.
- Incineration—TheNTP recommends purpose-built high-temperature incineration as the best environmental-friendly option for pharmaceutical destruction.
- Landfill—this implies putting waste directly into a land disposal site without prior treatment or preparation.

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