REPUBLIC OF KENYA

MINISTRY OF HEALTH

NATIONAL, TUBERCULOSIS, LEPROSY & LUNG DISEASE PROGRAM

GUIDELINE FOR INTEGRATED TUBERCULOSIS, LEPROSY AND LUNG DISEASE IN KENYA

SEPTEMBER 2017 EDITION

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ACRONYMS AND ABBREVIATIONS

A&C	Advocacy and Communication
AM	Amikacin
ARI	Acute Respiratory Infections
CHC	Community Health Committee
CHV	Community Health Volunteers
CM	Capreomycin
COPD	Obstructive Pulmonary Disease
CPT	Cotrimoxazole Preventive Therapy
Cs	Cycloserine
CXT	Cotrimoxazole
DM	Diabetes Mellitus
DOT	Directly Observed Therapy
DR-TB	Drug Resistant TB
DST	Drug Susceptibility Testing
E	Ethambutol
EPTB	Extra Pulmonary TB
Eto	Ethionamide
F	Female
FBF	Fortified Blended Flours
FDC	Fixed Dose Combinations
FFT	After failure of First Line Treatment
FRT	After failure of Retreatment
GERD	Gastroesophangeal Reflux
Gfx	Gatifloxacin
H	Isoniazid
HCWs	Health Care Workers
HIV	Human Immunodeficiency Virus
IDF	International Diabetes Federation
IGRA	Interferon Gamma Release Assay
ILDS	Interstitial Lung diseases
IPC	Infection Prevention and Control
IPT	Isoniazid Preventive Therapy
IYCN	Infant and Young Child Nutrition
Km	Kanamycin
LFX	Levofloxacin
LTBI	Latent TB Infection
M	Male
MAC	M. avium Complex
MDR TB	Multidrug Resistance
Mfx	Moxifloxacin
MTB	*Mycobacterium tuberculosis*
N	New
NACS	Nutrition Assessment Counselling and Support
NSA	Non State Actors
NSP	National Strategic Plan
NTLD-P	National Tuberculosis, Leprosy and Lung Disease Program
NTM	Non-tuberculous Mycobacteria
Ofx	Ofloxacin
PACS	Primary Care Asthma Control Screening Tool
PAL	Practical Approach to Lung Health
PAS	P-aminosalicylic acid
PCR	Polymerase Chain Reaction
PDR TB	Polydrug Resistance
PET	Positron Emission Tomography
PLHIV	People Living With HIV
PTB	Pulmonary TB
Pto	Prothionamide
R	Relapse
R	Rifampicin
RDU	Definition of Rational Drug Use
RR TB	Rifampicin Resistance
RUSF	Ready to Use Supplementary Foods
RUTF	Ready to Use Therapeutic Food
S	Streptomycin
SCHMT	Sub-County Health Management Team
SHS	Second Hand Smoke
SLE	Systemic Lupus Erythematosis
TB	Tuberculosis
TI	Transfer in
Trd	Terizidone
TSR	Treatment Success Rate
TST	Tuberculin Skin Test
TWG	Technical Working Group
WHO	World Health Organization
XDR TB	Extensive Drug Resistance
Z	Pyrazinamide

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FOREWORD

Tuberculosis remains a major cause of morbidity and mortality in Kenya. It affects all age groups, but has its greatest toll in the most productive age group of 15 to 44 years. The major factor responsible for the TB disease burden in Kenya is the concurrent HIV epidemic. Other factors that have also contributed to this include poverty and social deprivation that have led to mushrooming of peri-urban slums, congestion and limited access to general health services. With increasing trends of drug resistant TB cases, the fight against TB in resource limited countries like Kenya is a great challenge that requires concerted efforts from all stakeholders. To address challenges posed by the tuberculosis epidemic in the era of HIV, the Ministry of Health through the NTLD-Program has identified areas for increased support namely; Strengthening of human resources capacity at all levels for effective coordination of control activities, community engagement, strong collaboration between TB and HIV control programs to promote delivery of integrated TB/HIV services, promotion of private– public partnerships to increase the number of non - public providers integrated into the TB service provider network, sustained public health education campaigns to promote early care seeking and adherence to treatment at community level, and health care worker training and support for better TB case management.

This guideline is a revision of the earlier version produced in 2013 and has integrated all the individual guidelines from the different thematic areas. This easy to read version includes content on TB in special populations, newer technologies in diagnosis of TB, Social Protection, Poverty Alleviation, Gender and Human rights. The immediate short-term goal is to increase the detection of TB cases and sustain the successful treatment of those diagnosed. All these efforts are designed in a bid to achieve the end TB strategy goal of ending the global tuberculosis epidemic. The NTLD-P mandate also includes management of Leprosy which is in the post elimination phase in Kenya. However, there has been a significant gap in skills and knowledge by health care workers to suspect and diagnose the disease. This guideline includes an enhanced leprosy case management chapter with color plates and practical approach to case management. This guideline highlights key elements of lung disease to aid in its basic diagnosis and management. The incidence of respiratory diseases has continued to rise due to a rapid increase in a number of risk factors such as tobacco smoking habits in developing countries. The burden of asthma has increased worldwide and COPD is a frequent cause of disability and death. Kenya in an effort to improve the health of its population is strengthening the management of lung diseases through a number of approaches, key among them the Practical Approach to Lung Health (PAL) which entails use of standardized regimens, equipping and stocking facilities with necessary medicines and strengthening of community structures.

This guideline should therefore be used as the technical reference material by all health care workers involved in TB, Leprosy and Lung Disease care and can also be used for training of health care workers in conjunction with other training materials.

It is my sincere hope that all healthcare workers will find the integrated guideline useful for successful implementation of tuberculosis, Leprosy and lung disease control activities.

ACKNOWLEDGEMENT

The Ministry of Health and the National Tuberculosis, Leprosy and Lung Disease program (NTLD-P) are indebted to many individuals and organizations whose support and collaboration have made possible the updating of this edition of the national guidelines for the treatment and prevention of Tuberculosis for health workers.

We are grateful to CDC, KAPTLD, NASCOP, Moi University (AMPATH), University of Nairobi, Counties, WHO, CHS, MSF, HSO, Stop TB Partnership, PATH, MSH, KNH organizations whose staff put in much effort to ensure the success of this process. Special thanks goes to the NTLD-P staff who worked tirelessly in coordination and development of this guideline.

It is our sincere hope that the guidelines will be useful in improving prevention and case management of malaria in Kenya. By implementing the recommendations in the guidelines, there is no doubt that we shall reduce malaria related illnesses and deaths and put Kenya on the path towards a Tuberculosis free future.

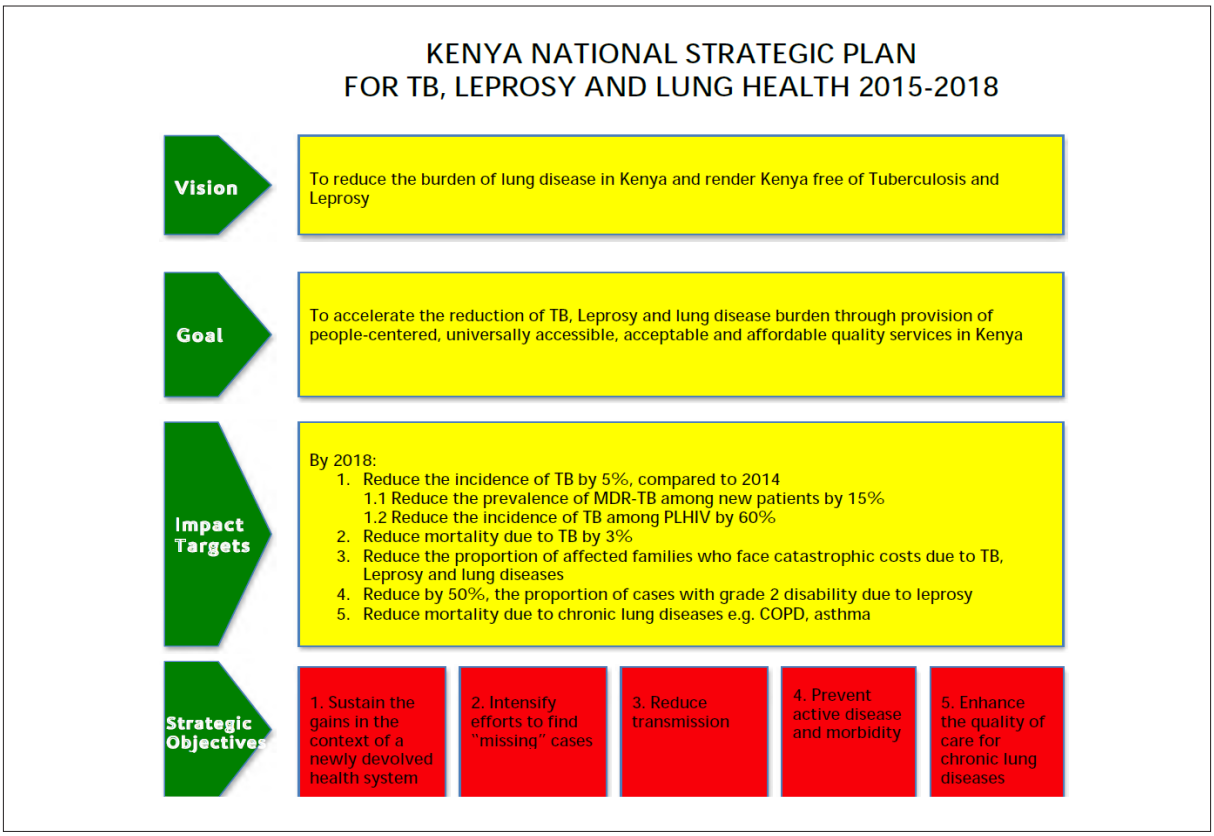
CHAPTER 1

INTRODUCTION

Introduction to the Integrated Curriculum for Tuberculosis, Leprosy and Lung Disease

The Ministry of Health has a vision to reduce the burden of lung disease in Kenya and render Kenya free of TB and leprosy. The National Tuberculosis, Leprosy and Lung Disease Program (NTLD Program) is mandated to develop policies, build capacity and provide technical assistance to the devolved county system in relation to lung Health and leprosy in Kenya. The NTLD-Program implements its activities within the framework of the National Strategic Plan for Tuberculosis, 2015-2018. The main elements of this strategic plan are summarized in Figure 1.1.

Figure 1.1: Kenya National Strategic Plan for TB, Leprosy and Lung Health 2015-2018



Respiratory diseases are responsible for a considerable burden of suffering and death in all age groups worldwide. Respiratory diseases have always been an important cause of morbidity and mortality. In recent decades, their incidence has continued to rise which can be attributed to a rapid increase in a number of risk factors such as tobacco smoking habits in developing countries, the HIV epidemic, urbanization, industrialization, atmospheric pollution, and the deterioration of socioeconomic conditions.

Respiratory symptoms are the most frequent complaints among those visiting outpatient services. The most frequently occurring respiratory diseases that result in significant morbidity and mortality are pneumonia, acute respiratory infections (ARI), Tuberculosis, asthma, chronic obstructive pulmonary disease (COPD) and lung cancer.

Kenya is making efforts to improve the health of its population through strengthening of the management of lung diseases under Practical Approach to Lung Health (PAL) which entails use of standardized regimens for Lung disease, training of health care workers, equipping facilities and stocking them with necessary commodities. It also involves strengthening of community structures to support the delivery of essential health interventions as an integral part of primary health care. PAL therefore is a syndromic approach to the management of patients who attend primary health care services with respiratory symptoms and improve the quality management of respiratory patients aiding in early diagnosis of tuberculosis.

It is estimated that one third of the world's population is infected with *Mycobacterium tuberculosis (M.TB),* the bacterium that causes tuberculosis (TB). Each year, about 9 million people develop TB globally, of whom, approximately 2 million die. Of the 9 million annual TB cases, about 15% occur in children under 15 years of age. Of the childhood cases occurring annually, 75% occur in the 22 high-burden countries that account for 80% of the world's estimated incident cases. Kenya is among the 22 TB high TB burden countries in the world and is among the top 5 countries with the highest TB burden from sub Saharan Africa.

In 2015, Kenya reported 81,232 cases of all forms of TB with 8.5% of all cases notified being children below15 years of age. The case notification rate is 210/100,000 population. In the last 5 years, Kenya has reported an annual decline in the number of reported TB cases at a rate of 1%. There has been a general increase in the proportion of bacteriologically confirmed cases with the advent of increasing utilization of MTB/RIF assay (gene Xpert) testing in the country.

Drug resistant tuberculosis continues to be a major public health challenge in Kenya with an increasing case notification of different forms of drug resistance TB cases every year. Globally, it is estimated that 480,000 cases developed MDRTB in 2014. This is approximately 5% of all TB cases. In 2015, a total of 408 DR TB cases were diagnosed and enrolled on treatment. Surveillance of DR TB has continued to be strengthened with the use of gene Xpert testing to diagnose tuberculosis and identify Rifampicin resistance.

Pulmonary diseases with nutritional implications include TB, COPD, Asthma, Pneumonia, bronchitis, among others. Poor nutrition in lung disease has been related to adverse effects that may contribute to complications and increased mortality. Malnutrition markedly increases mortality among both TB and HIV/AIDS patients and should be managed concurrently with treatment of these infections. Nutritional status is one of the most important determinants of resistance to infection. It is well known that there is a close association between TB and malnutrition as malnutrition increases the risk of developing TB and the vice versa.

Globally over 215,000 leprosy cases were notified in the year 2013 with majority of leprosy patients being found in South East Asia, the Americas and Africa. Despite being in the post elimination phase, Kenya notified 133 cases. Majority (90%) of these cases were multi-bacillary (infectious type). Leprosy endemic counties include Kilifi, Kwale, Malindi, Kisumu, Siaya and Busia. Despite the apparent low number of cases reported annually in Kenya, 11% of the cases notified in 2014 were notified in patients below 15 years of age. This suggests stable active transmission of leprosy in the community.

Though diagnosed and managed within the formal health system, TB and Leprosy thrive in the community. It is therefore important to link community activities for TB and Leprosy with the work of NTLD-P so that efforts of the health systems are extended and reach as many people as possible, and also create demand for quality services. This calls for enhanced collaboration and coordination between the health care workers, communities and non-state actors, in order to realize universal coverage and comprehensive care in TB, leprosy & Lung Health services.

The current advocacy and communication strategies identify the need to create an enabling environment for prevention lung diseases. Advocacy will target those in positions of authority to influence human, financial and material resources to strengthen the fight against TB, Leprosy and other lung diseases. Additionally, community advocacy takes advantage of community-level structures such as community health volunteers to create public demand for TB, leprosy and lung disease services. In this regard, health care providers are crucial channels of advocacy and communication while at the same time being targeted with messages to counter the risks arising from occupational hazards.

Case recording and reporting of TB, leprosy and other lung disease is an important process for monitoring and evaluating disease control activities at the health facility, county and national levels. Accurate, complete and timely data collection is an overarching guiding principle for the program. Every health care provider who treats TB, leprosy and other lung disease has the professional responsibility to record and report all cases treated using standardized tools provided by the program, while the national TB program is responsible for providing standardized recording and reporting tools which should be used at all service delivery points. This in turn is aggregated at national level to establish how well the NTLD-P is closer to achieving the currently set programmatic performance indicators set in Table 1;

Table 1.1: Some Performance Indicators for NTD-Program

Some Performance Indicators for the NTD-Program	Target
Treatment Success Rate (TSR)	90%
HIV Testing and Counseling for TB patients	100%
Antiretroviral for TB/HIV co infected patients	95%
TB screening for People Living with HIV	100%
Children <5 years with contact to TB initiated on IPT	100%
CTX/dapsone for co-infected	100%
IPC- Presence of functional IPC workplan, HCW screening in every facility	100%

Scope of the guidelines

The overall objective of these guidelines is to provide a public health approach to the management of TB, Leprosy and Lung disease. These guidelines are expected to give guidance to health care workers (HCWs) on the diagnosis, treatment, prevention and rehabilitation of patients with these conditions.

Target audience

The guidelines are targeted to all HCWs of various cadres who manage TB, Leprosy and Lung disease. They will also be of use to those undergoing pre service clinical training. They will assist the county managers who are tasked with the planning and resource allocation to ensure the needs of these patients. They will also assist policy makers and other line ministries in the national government working in areas of health, social services, prison services or immigration in decision making related to tuberculosis, leprosy and lung disease. The guidelines will be a reference for all partners and organizations that are involved in the management of these patients.

Rationale for Integrated Tuberculosis, Leprosy and Lung Disease Guidelines

The National strategic plan for Tuberculosis, Leprosy and Lung Health 2015-2018 outlines a need to reduce the number of reference tools that health care workers use in the management of patients with TB, Leprosy and Lung Disease. The review and integration of the various guidelines into one ensure that these guidelines are user friendly. An integrated training curriculum for TB, Leprosy and Lung Disease has been developed to build the capacity of health care workers on the content of these guidelines.

Organization of the Integrated TB, Leprosy and Lung Disease Guidelines

These guidelines are organized into the following sections:

1. Practical Approach to Lung health: The syndromic approach to the management of patients attending primary health care services with respiratory symptoms in order to improve early diagnosis of tuberculosis.
2. This section includes the diagnosis and treatment of all forms of tuberculosis in children, adults and other special populations.
3. Nutrition: This section highlights the relationship between nutrition lung diseases.
4. Advocacy Communication and Social mobilization in relation to tuberculosis, leprosy and lung disease.
5. Infection Prevention and Control of Tuberculosis.
6. Leprosy; Case detection and management of leprosy.
7. Commodity Management:, commodity management and management of adverse drug reactions (pharmacovigilance).
8. Monitoring and Evaluation; This highlights the processes and tools involved in the accurate recording and reporting TB leprosy and lung disease activities and interventions within the program.

CHAPTER 2

LUNG DISEASES

A) Introduction

Background

Respiratory diseases are responsible for a considerable burden of suffering and death in all age groups worldwide. Respiratory diseases have always been an important cause of morbidity and mortality. In recent decades, their incidence has continued to rise which can be attributed to a rapid increase in a number of risk factors such as tobacco smoking habits in developing countries, HIV epidemic, urbanization, industrialization, atmospheric pollution, and the deterioration of socioeconomic conditions.

Respiratory symptoms are the most frequent complaints of those visiting outpatient services The most frequently occurring respiratory diseases that result in significant morbidity and mortality are pneumonia, acute respiratory infections (ARI), TB, asthma, chronic obstructive pulmonary disease (COPD) and lung cancer. The burden of asthma has increased worldwide both in adults and children with marked increase in children in developing countries over the past five years. COPD is a frequent cause of disability and death worldwide.

Burden of respiratory diseases in Kenya

Adult respiratory diseases in the developing world are a major burden and the morbidity and mortality; particularly that related to chronic respiratory diseases, are of increasing concern. These diseases fall into four categories:

- Acute diseases, such as pneumonia and influenza;
- Chronic obstructive pulmonary disease (COPD) and asthma;
- Occupational lung diseases, such as asbestosis, and coal worker's pneumoconiosis
- Other parenchymal lung diseases, such as immune-related lung diseases and lung cancer

For many years, the leading cause of adult respiratory disease mortality has been tuberculosis, which still kills far more people than it should, given the increased efficacy of treatment and preventive regimens. The burden of chronic adult respiratory diseases, which has been rising throughout the world, is however unmeasured mainly due to reporting gaps. While it may not be necessarily possible or desirable to include details of all the respiratory conditions in

this guideline, key elements of each diseases are included here to aid basic diagnosis of most respiratory diseases. Most of the diseases have been addressed in other Ministry of Health guidelines which will serve as references for this document.

Kenya in an effort to improve the health of its population is strengthening the management of lung diseases through a number of approaches, key among them the Practical Approach to Lung Health (PAL). This entails use of standardized regimens for Lung disease, training of health care workers, equipping and stocking facilities with necessary medicines. It also involves Strengthening of community structures to support the delivery of essential health interventions as an integral part of primary health care.

Figure 2.1: Burden of Respiratory Disease Globally

Percentage of deaths	2008	2015	2030
Lower respiratory infections	6.1	5.5	4.2
COPD	5.8	6.6	8.6
Trachea/bronchus/lung cancer	2.4	2.8	3.4
Tuberculosis	2.4	1.6	3.4
Percentage of DALYs	**2008**	**2015**	**2030**
Lower respiratory infections	5.4	4.6	3.2
COPD	2.3	2.7	3.8
Trachea/bronchus/lung cancer	0.9	1.0	1.4
Tuberculosis	2.0	1.6	1.1

Source: Projected proportion of deaths & DALYs due to leading respiratory causes- WHO statistics 2011

Strategy for managing respiratory diseases in Kenya

a. The Practical Approach to Lung Health (PAL) strategy

In PHC settings, clinical symptoms presented by pulmonary TB patients are, in general, similar to those symptoms displayed by non-tuberculosis respiratory patients, particularly those with persistent symptoms. PAL is a syndromic approach to the management of patients who attend primary health care services with respiratory symptoms and improve the quality management of respiratory patients aiding early diagnosis of tuberculosis. PAL strategy targets health care workers in particular, nurses, clinicians and managers in primary health care settings. The program employs the PAL (strategy) approach in managing respiratory illnesses in Primary Health Care setting.

PAL is aimed at improving the management of major respiratory disorders in patients over 5 years (who are not catered for in the IMCI guidelines), and in the process increase the identification of TB patients among all those with compatible symptoms. Clinical services at PHC facilities include curative, disease prevention and health promotion. Health education is important to ensure long-term treatment adherence and promote safe behavior. Health education should:

(i) Ensure that TB patients adhere to treatment and the process of screening & examination of their contacts

(ii) Ensure that asthma and COPD patients stick to self-medication(prescribed) regimes and

(iii) Learn how to adequately perform inhalation procedures for self-care and when to seek care

(iv) Help asthma patients identify and avoid their asthma attack-triggers

(v) Educate all respiratory patients on the effects of smoking and encourage them to quit

(vi) Promote prevention of tobacco use among respiratory patients in PHC settings

b. Level 4 - Level 5 health care facilities

While the diagnosis of respiratory illnesses at PHC setting is symptom based, the PAL strategy in the referral Level need to go beyond symptoms to include critical diagnostics.
In this guideline, the lung diseases addressed include:

1. Acute respiratory illnesses specifically pneumonia
2. Chronic lung diseases
    a. Tuberculosis
    b. Asthma
    c. COPD
    d. Others: interstitial lung disease and Lung Cancer

B) Pneumonia

Pneumonia is an infection of the lung parenchyma and can be classified as:

1. Community-acquired pneumonia, acquired outside hospitals settings or extended-care facilities
2. Hospital acquired pneumonia refers to lung infection acquired in hospitals.

Signs and symptoms of acute pneumonia develop over hours to days, whereas the clinical presentation of chronic pneumonia often evolves over weeks to months.

Pathophysiology

Six mechanisms have been identified in the pathogenesis of pneumonia in immunocompetent adults. Inhalation of infectious particles is probably the most important pathogenic mechanism in the development of community-acquired pneumonia.

Causes of pneumonia

- Typical pathogens
  - Streptococcus pneumonia
  - Staphylocccus aureus
  - Klebsiela pneumonia
  - Haemophylus influenza
- Atypical pathogens
  - Mycoplasma pneumonia
  - Legionella pneumonia
- Respiratory viruses
  - Influenza virus
  - Adeno virus
  - Respiratory Syncytial Virus

Pathogenic mechanisms of pneumonia

- Inhalation of infectious particles
- Aspiration of oropharyngeal or gastric contents
- Hematogenous deposition
- Invasion from infection in contiguous structures
- Direct inoculation
- Reactivation

Clinical Presentation of Pneumonia

- Breathlessness
- Cough with or without sputum (which may be rust colored)
- Fever
- Sharp, stabbing, burning or dull pain on the left or right side of the chest
- Bronchial breathing
- Reduced chest movement
- Reduced breath sounds
- Rapid breathing
- Crackles and dullness on percussion

Differential Diagnosis of pneumonia

- Acute exacerbation of COPD
- Heart failure
- Pulmonary embolism
- Radiation pneumonitis
- Acute Bronchitis

Investigation

- Full heamogram
- Peripheral blood film
- Sputum microscopy
- Chest X-Ray
- Blood slide for MPS

Management of pneumonia

Outpatient management

- Crystalline penicillin 2 mega units stat then Amoxicillin 500mg 8hly 5-7days,
- If allergic to penicillin give erythromycin 500mgs 6hly 5-7days or Cotrimoxazole 960mg twice daily with plenty of water.
- Give analgesics (Paracetamol 1gm 8hly or Ibuprofen 400mg 8hly for 3 days) for fever and pain if indicated.

Inpatient management

- Crystalline penicillin 2 mega units 8 hourly and Gentamycin 160mg once daily for 5days
- or Ceftriaxone 2gms daily 5 days
- If allergic to Penicillins give erythromycin 500mgs 6hly for 10 days.

Management of aspiration pneumonia:

- Metronidazole 400mg 8hly for 5-7 days and Augmentin 625mg twice daily for 5-7 days

Staphylococcus infection

- Flucloxacillin 500mg 6hly for 5-7 days

Prevention of Pneumonia

- Vaccinations
- Hand washing with soap,
- Reducing household air pollution,
- HIV prevention and cotrimoxazole prophylaxis for HIV-infected and exposed children

Note: *For treatment of pneumonia in children less than five years refer to the National IMCI guidelines*

C) Introduction to Chronic Lung Diseases

This guideline focuses on the following Chronic Lung Diseases:

1. Tuberculosis
2. Asthma
3. COPD
4. Lung cancer
5. Interstitial lung diseases

Causes of a chronic cough

- Asthma
- Tuberculosis
- Chronic Obstructive Pulmonary Disease (COPD)
- Interstitial Lung diseases
- Bronchiectasis
- Lung cancer
- Left heart failure
- Idiopathic cough
- Chronic allergic rhinitis
- Gastroesophangeal reflux (GERD)
- Side effects of certain medicines e.g. ACE I

D) Asthma

Asthma is defined as **heterogeneous disease**, usually characterized by chronic airway **inflammation**. It is characterized by a history of **respiratory symptoms which include wheeze, shortness of breath, chest tightness and cough** that vary over time and intensity, together with variable expiratory airflow limitation.

The components of asthma definition must be present:

- Heterogeneity
- Chronic airway inflammation
- Recurrent or persistent symptoms of cough, wheeze, chest tightness and breathlessness
- Wide spread but variable and reversible airways obstruction

Burden of disease: It is estimated that 300 million people suffer from asthma globally. In Kenya it is estimated that 3-4 million people suffer from asthma accounting for about 10% of the Kenyan population.

Pathophysiology: The characteristic pathophysiologic effect of the airway inflammation is airway hyper-responsiveness and airway narrowing from airway smooth muscle contraction, overproduction of airway mucus, airway edema and the airway remodeling from deposition of collagen in the basement membrane. The pathological and pathophysiologic changes in asthma are and risk factors are summarized.

Summary of Airway Pathophysiologic Processes in Asthma

- Airways Inflammation with increased number of activated inflammatory cells
- Production of various chemical mediators (mediator soup)
- Airway structural changes resulting from the airway inflammatory process
- Airway functional changes (Airway Hyper-responsiveness) from the inflammatory process and structural changes
- Airway Narrowing from airway smooth muscle contraction, airway thickening from collagen deposition, airway edema and excessive airway.

Table 2.1: Risk factors for asthma

Non Modifiable Factors	Modifiable Factors	Environmental factors
• Gender: - Early M>F - Later F>M • Atopy • Airway Hyper responsiveness	• Allergen Exposure • Infections and Infestations • Breastfeeding • Air pollution • HIV infection • Occupational Exposures • Tobacco smoking including environmental tobacco smoke(passive smoking)	• Indoor allergens • House dust mite (*Dermatophagoides* spp) • Animal allergens (Cat, Dog, Rodents) • Cockroaches • Fungi – molds especially A*lternaria* • Outdoor allergens • Pollens from trees, grasses and weeds • Fungi – *Alternaria* and *Cladosporium* • Occupational sensitizers: e.g. isocyanates in spray paints • Tobacco smoke – parental smoking in children • Air pollution- Industrial smog (sulphur dioxide particulate) and photochemical smog (ozone and nitrogen oxides) • Indoor pollutants – sulphur dioxide, carbon dioxide, carbon monoxide, nitrogen oxide, nitric oxide.

Diagnosis of Asthma

General diagnostic principles

An accurate diagnosis of asthma is essential to enable the provision of appropriate treatment. The clinical history is the most important element in the diagnostic process for asthma.
A diagnosis of asthma should be considered in all patients who present with episodic or persistent wheeze, shortness of breath, chest tightness and cough.
Presence of wheeze on chest auscultation may enhance the clinical confidence with which the diagnosis of asthma is made; the absence of wheeze on chest auscultation should not be used to exclude asthma.

Table 2.2: Typical and atypical presentation of asthma

Typical presentation	**Atypical presentation**
• Frequent episodes of wheezing, cough and breathlessness vary in duration and severity • Symptoms occur mainly at night and wake up patient, usually in the early hours of the morning • Disappear spontaneously or after bronchodilator use • Persistent breathlessness can occur in the most severe form of asthma, due to progression from reversible to irreversible airflow limitation • Severe progression is rare and linked to irreversible airway fibrosis • Several risk and trigger factors usually present	• Mainly in children • Recurrent attacks of cough, particularly in the evening and/or at night, which do not respond to symptomatic treatment • Chest tightness with wheezing that occurs only after exercise • Clinical pattern similar to an acute respiratory infection but frequently recurs during a short period

It is recommended that all adult patients suspected or known to have asthma have a spirometric lung function test. The measurement of lung function testing with spirometry or peak expiratory flow measurement with a peak flow meter may enhance the diagnosis of asthma, provide an indication of disease severity and help distinguish asthma from chronic obstructive pulmonary disease(COPD) or other diseases that present with cough, wheeze and shortness of breath. If the clinical suspicion of asthma remains high but lung function testing is normal, it is recommended that airway hyper-responsiveness be measured.

Classification of asthma

The classification is based on severity of disease thus; Intermittent, mild persistent, moderate persistent and severe persistent asthma.

Table 2.3: Classification of Asthma

Classification	Symptoms	Nocturnal symptoms	PEF or FEV
Intermittent	< 1 time week Asymptomatic and normal PEF between attacks	≤ 2 times a month	≥80% predicted Variability < 20%
Mild persistent	> 1 time a week, but < 1 time a day	> 2 times a month	≥ 80% predicted Variability 20 - 30%
Moderate persistent asthma	Daily Attacks affect activity	> 1 time week	60 - 80% predicted Variability > 30%
Severe persistent asthma	Continuous Limited physical activity	Frequent	≥60% predicted Variability > 30%

How to diagnose asthma

Listen to the patient*(the clinical history is the most important in the diagnosis of asthma)*

- Is there recurrent or episodic wheeze, cough, chest tightness or shortness of breath?
- Are the symptoms particularly troublesome at night or early morning?
- Are the symptoms triggered by factors such as dust, cold exposure, strong smells or exercise?
- Is there a consistent response to asthma specific treatment?

Obtain a lung function Test (measure FVC, FEV1 and PEF) by Spirometry

- Is there airflow limitation (FEV1/FVC% less than 80?)
- Is there a bronchodilator response (FEV1 or PEF improved by greater that 20%, 30 minutes after inhalation of a short acting bronchodilator)?
- Measure PEF variability (wide swings in the PEF between morning and evening or when at work and off work)
- Measure airway hyper-responsiveness
- Does the FEV1 drop below 20% with only small doses of an inhaled bronchoconstrictor such as Methacholine, Histamine or with exercise?

Diagnosis of asthma in children

The general principles for the diagnosis of asthma apply to children

- Relies on clinical suspicion, physical examination and trial of asthma treatment.
- It is highly suggestive in the presence of frequent episodes of wheeze (more than once a month), can be activity induced cough or wheeze and cough with or without wheeze in the absence of a viral respiratory tract infection.
- A strong family history of asthma or allergic disease is also supportive of the diagnosis of asthma in very young children.

Consider asthma if the child has the following:

- Frequent episodes of wheeze, cough, chest tightness, breathlessness particularly experienced at night, early morning, or in response to exercise, common allergens, emotions, laughter or occur in the absence of 'common cold'
- Personal history of atopy or Family history of atopy and or asthma
- Wide spread wheeze on chest auscultation
- History of improvement in symptoms or lung function in response to asthma specific therapy

Differential diagnosis of asthma:

Adults	• Tuberculosis • Chronic bronchitis and COPD • Heart disease • Hyperventilation syndrome • Bronchiectasis
Children	• Acute respiratory infection • Foreign body inhalation • Bronchiectasis

Table 2.4: Primary care Asthma Control Screening tool (PACS)

Have you experienced any of the following more than once a week in the last month?	*Yes*	*No*
Symptoms of asthma, cough, wheeze, shortness of breath		
Waking at night because of asthma		
Chest tightness on waking		
Difficulty in performing vigorous activity like running, lifting heavy objects, exercise		
Difficulty in performing moderate activities like vacuuming, climbing flights of stairs		

Management of asthma

The aim of management is to achieve asthma control and to return patients to productive lives.

Goals of asthma care/management are to:

- Achieve and maintain control of symptoms
- Prevent asthma exacerbations
- Maintain lung function as close to normal as possible

- Maintain normal level of activity including exercise
- Avoid adverse effects of asthma medications
- Prevent development of irreversible airflow limitation
- Maintain normal growth velocity in children
- Prevent asthma mortality

Asthma Medications are classified into two broad groups:

Relievers	They reverse Broncho-constriction and relieve its symptom. They include rapid and short acting, rapid and long acting or slow and long acting.
Controllers	They are taken daily to keep asthma under control through their anti – inflammatory effects.

NB : Long Acting B2 Agonists (LABA) have anti-inflammatory effect, are used in combination with inhaled corticosteroids for the long term control of asthma, they also inhibit mast cell mediator release, plasma exudation and reduce sensory nerve activation.

- It must be emphasized that anti-inflammatory therapy (ICS) forms the backbone of asthma control
- All asthma patients except those with very mild and intermittent symptoms should be on inhaled corticosteroids

Management of Acute asthma

Acute asthma is classified as: Mild asthma attack, Moderate asthma attack and severe asthma attack.

Assessment of patient with acute asthma attack:

- **Step 1:** Assess for signs of imminent respiratory arrest.
- **Step 2:** If there are no signs of imminent arrest, assess for signs of clinical distress.
- **Step 3:** If the patient is not in imminent arrest, proceed with assessment and treatment in the emergency room

Management of asthma exacerbations (Acute Severe Asthma)

Asthma exacerbations are progressive worsening of asthma symptoms. They are episodes that come on suddenly and may recur from time to time. They often come on at night. They can occur in a patient whose asthma is well controlled, but often indicate a failure in the long-term management

The three critical elements of treating an asthma exacerbation include:

- Rapid achievement of bronchodilation
- Early administration of systemic steroids
- Oxygen supplementation.
- Continuation of treatment and monitoring
- Discharge or hospitalization

Management of severe asthma

- Oxygen
- Bronchodilators: Inhaled Salbutamol: 4 - 8 puffs every 20 minutes for 1st hour, then every 2 hours
- Systemic corticosteroids: Oral prednisone at a dose of 0.5-1 mg /kg /day

Treatment continuation and Monitoring

- Keep patient in the emergency room for at least 6 hours
- Verify the patient's state every 20 minutes during the first hour
- Evaluate PEF

Management of moderate asthma

- Inhaled salbutamol 2 - 4 puffs every 20 minutes for the first hour
- oral prednisone at a single dose of0.5-1 mg / kg / day

Discharge

- Complete response (disappearance of clinical signs and PEF ≥ 80%)
- Stable at 1 hour after last dose of salbutamol, the patient can be discharged
- No response or incomplete response (no or incomplete disappearance of clinical signs or PEF < 80%)
  - patient treated as for a severe attack

Conditions for discharge

- Identify and avoid the cause of the attack;
- Verify that inhalation technique is correct;
- Provide a prescription that includes inhaled beta2-agonists and a short course of oral corticosteroids to prevent relapse;
- Arrange follow-up at the health centre where the patient is registered
- Prior to leaving the emergency service, health care providers must outline with the patient a clear plan of follow-up.
- Patients should be able to recognize the signs of deterioration and to treat the episodes themselves as soon as the first clinical signs of an attack appear.

Management of mild asthma

- Treat the patient as an outpatient
- Initial treatment - inhaled salbutamol 2 - 4 puffs every 20 minutes for the first hour. If there is complete response (i.e. disappearance of clinical signs and PEF ≥ 80%) and stable at 1 hour after last dose of salbutamol, discharge patient on daily controller and reliever medications
- If there is no response or incomplete response (i.e. no or incomplete disappearance of clinical signs or PEF < 80%), treat as moderate asthma attack

Management of Chronic asthma

- Bechlometasone, Fluticasone, Budesonide (Controllers /preventers inhaled medicines)

Other drugs used in asthma management

Theophyllines	These are Short acting i.e. Aminophylline it may be used to relieve bronchospasm in asthma
Anti-cholinergics	They are used for the treatment especially in the acute care setting. Ipratropium bromide it is usually combined with a short acting B2 agonist.
Leukotriene Modifiers	They are used as add on therapy in patients who fail to achieve control. Used with low dose inhaled corticosteroids or as alternatives to low dose inhaled corticosteroids and in aspirin induced asthma (AIA). It is useful in the presence of allergic rhinitis and asthma to relieve both nasal and chest symptoms.
Systemic Corticosteroids	They are recommended for patients with moderate to severe acute exacerbations of asthma. In some patients with steroid dependent asthma the lowest possible dose of should be used.
The cromones, Anti IGE	Refer to the National asthma Guidelines

Seasonal asthma

- Seasonal asthma is often linked to a pollen allergy
- Determine severity of asthma according to symptom frequency during that particular season
- Prescribe corresponding long-term treatment for patient to take during that season

Routine care for asthma patients

Asthma is a chronic illness and therefore the clinical team and patients need to develop a long term plan for the patient management
The Patient – Health Provider Partnership include;

1. Personalized Education: Ensure the following is included in the patient education;
   a. Basic information about the Disease
   b. Medication including Relievers and Preventers
   c. Potential side effects of medicines
   d. Training on the medicine inhaler technique
   e. Recognition of worsening asthma and actions to be taken
2. Self-monitoring of asthma control
   a. Regular review to assess control and adjust treatment as may be necessary
   b. Identification and avoidance of symptom trigger factors (indoor and outdoor pollutants)
3. A written asthma management plan

E) Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Airway Disease is a term used to describe progressive lung disease that makes it hard to breathe. It includes chronic bronchitis and Emphysema. It is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases {*Ref. Global strategy for the diagnosis, management, and prevention of Chronic Obstructive Pulmonary Disease updated 2015*}.

Causes/risk factors

- Active Tobacco smoking
- Secondary tobacco smoking
- Indoor air pollution due to the use of bio fuels and coal for cooking
- occupational dusts and chemicals
- frequent lower respiratory tract infections during child birth
- post Tuberculosis- lung damage

Diagnosis of COPD

Consider COPD in a patient with;

- Dyspnea that is progressive, persistent and worsens with exercise
- Chronic cough which maybe intermittent and productive or not productive
- Chronic sputum production
- Chronic sputum production
- Wheezing
- History of exposure to risk factors which may include; tobacco smoking, smoke from home cooking and heating bio fuels, occupational dusts and chemicals

Patient with above symptoms and previously treated for Tuberculosis

- Age of 40 years and above
- Family history of COPD

Lung function testing: Spirometry

The table below summarizes the lung function measurements that are key to making a diagnosis of airflow limitation in COPD

- Spirometry is the Gold standard for clinical diagnosis and monitoring COPD.
- post bronchodilator FEV_1/FVC less than 70% confirms the presence of persistent airflow limitation
- To diagnose, manage and follow up COPD patients one should have access to Spirometry facilities.

Distinguishing asthma and COPD: Practical approach to diagnosis of COPD

A patient with a chronic cough may have more than one disease. In case of a chronic cough, first exclude TB, lung cancer, chronic bronchitis, heart failure and post infectious cough. Then consider asthma or chronic obstructive pulmonary disease (COPD) which both present with cough, difficulty in breathing, tight chest and wheezing

If the cause of wheezing is not known, distinguish COPD and asthma as follows:

• Onset before 20 years of age • Associated hay fever, eczema, allergies • Intermittent symptoms, with normal breathing in between • Symptoms worse at night, early morning, with cold or stress • Personal or family history of asthma **Asthma likely** Confirm diagnosis - Give routine asthma care	• Onset after 40 years of age • Symptoms are persistent and worsen slowly over time • Cough with sputum starts long before difficult breathing • Client is or was a heavy smoker and had TB • Previous doctor diagnosis of COPD **COPD likely** Confirm diagnosis - Give routine COPD care

Management of COPD

A. Assessment of COPD severity and risk of exacerbation

The assessment is aimed at determining disease severity, its impact on patient's general health status, risk of exacerbations and death. Suggested further reading GOLD guidelines on COPD}.

Classification of severity of COPD based on Post bronchial FEV1/FVC (GOLD: COPD guidelines)

GOLD 1	Mild COPD	$FEV_1 \geq$ 80% predicted
GOLD 2	Moderate COPD	50% ≤ FEV_1 < 80% predicted
GOLD 3	Severe COPD	30% ≤ FEV_1 <50% predicted
GOLD 4	Very severe COPD	FEV_1 < 30% predicted

Asses risk for exacerbations

Exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond the normal day-to-day variations and leads to a change in medication. The best predictor of frequent exacerbations (2 or more per year) is a history of previous treated events

Management of COPD

Goals of COPD management

- To relieve symptoms
- Prevent disease progression
- Prevent and treat complications and exacerbations
- Reduce risk of dying

Treatment of COPD

1. Smoking cessation: This is has the greatest impact in reducing the disease progression. This can be done through
    a. Patient counseling
    b. Nicotine replacement therapy e.g. nicotine patches, nicotine gums, sublingual tablets etc. (*refer to tobacco cessation section for more details*)

    Institution of smoking prevention and tobacco control strategies *(refer to National tobacco control policies)*
2. Prevention of occupational exposure
3. Reduction of exposure to indoor pollutants e.g. bio fuels in poorly ventilated houses
4. Physical exercise
5. Pharmacotherapy – the drugs used in the management of COPD are aimed at reducing symptoms, frequency and severity of exacerbations and improving health status. They include
    a. Inhaled bronchodilators
    b. Inhaled corticosteroids
    c. Combined inhaled corticosteroid/ bronchodilator therapy is more effective than individual components

    Antibiotics are not recommended except for treatment of suspected bacterial infections
    d. Mucolytic agents for patients with viscous sputum
    e. Oxygen therapy. Long term administration of oxygen for > 15 hours per day has been shown to increase survival in patients with severe COPD
    f. Palliative care/ hospice care is important for patients with advanced COPD which is marked with deteriorating health status, increasing symptoms, frequent acute exacerbations with frequent hospitalizations and associated co morbidities e.g. cardiovascular diseases, malignancies and progressive respiratory failure

Table 2.5 shows a guide for management of COPD based on severity of the disease.

Table 2.5: A Guide for Management of COPD Based on Severity of the Disease

COPD severity classification	Mild COPD	Moderate COPD	Severe COPD
Inhaled beta agonist	2puffs when needed (up to 4 times a day)	2 puffs when needed (up to 4 times a day)	2 puffs when needed (up to 4 times a day)
Inhaled Ipratropium bromide		2 puffs when needed (up to 4 times a day)	2 puffs when needed (up to 4 times a day)
Combination long acting beta agonist and anticholinergic in one inhaler			
Inhaled cortico steroid			
Combination inhaled corticosteroid and agonist in one inhaler			
Slow release theophylline (Hospital level)			200-300mg twice day taken long term.

Routine COPD care

The aim of COPD care is to stop further deterioration of lung function and to recognize and treat acute exacerbations early. COPD patients need to be reviewed regularly. At each visit provide the following care:

- Smoking cessation: This is the mainstay of care. Smoking cessation drastically reduces the progression of disease. People are more likely to stop smoking if advised by a health professional
- Assess severity of COPD and treat according to severity
- Ensure optimal delivery of drugs by educating patients on correct use of inhalers. Check adherence to treatment and inhaler/spacer technique.
- Treat infective exacerbations. LRTIs occur commonly in patients with COPD. In patients previously treated for Tuberculosis, repeat TB tests only if other TB symptoms develop. If patient's sputum increases or changes in color to yellow/green, treat for LRTI:
    - Give doxycycline 100mg 12 hourly for 10 days or amoxicillin 500mg 8 hourly for 10 days.
    - Give short course oral prednisone 40mg daily for 7 days if patient has severe COPD
    - High dose (800pg) inhaled corticosteroids are effective in patients with severe COPD with more than 2 infective exacerbations per year
- Give influenza vaccine yearly and pneumococcal vaccine 5 yearly
- Identify and manage complications. Treat fluid retention with a low dose diuretic.
- Encourage patient to exercise daily e.g. walking, gardening, household chores, using stairs instead of lifts etc.
- Review patients every 3-6 months if stable.

F) Interstitial Lung Diseases (ILDs)

Interstitial Lung diseases (ILDs) also referred to as diffuse parenchymal lung diseases are a group of chronic conditions that generally present with the symptom of breathlessness. They lead to lung tissue damage and ultimately fibrosis or tissue scarring with loss of the lung tissue elasticity. The lung loses its ability to supply oxygen to the blood stream and as the scarring progresses, one loses ability to breath.

Pathophysiology

The underlying pathology in the conditions is inflammation with or without fibrosis of the alveolar walls which cause impaired gas exchange. The ILDs usually have a gradual onset but can also present an acute onset.

Causes of ILDs

The ILDs are classified into those of known cause (about 35%) and those whose causes are unknown (about 65%).

Causes of ILDs

For those with known cause, some known causes include:

1. Environmental factors which include exposure to air pollutants. These include long term exposure to asbestos, allergens e.g. from birds causes hypersensitivity pneumonitis/ Extrinsic Allergic Alveolitis
2. Autoimmunity- one's own immune system attacks their body. This causes diseases with generalized effects in the body which include the lungs. Some of these include; Dermatomyositis, rheumatoid Arthritis, Polymyositis, Systemic Sclerosis/ Scleroderma, Systemic Lupus Erythematosis (SLE). Chest symptoms maybe the first signs/symptoms of these autoimmune diseases long before other organ symptom manifestations.
3. Drug reactions. Some drugs have been reported to cause ILDs in a small group of people who take them over a long period of time. Some include; nitrofurantoin, Amiadorone
4. Sarcoidosis
5. Genetics

Some of the common ILDs include:

1. Those of known causes;
    a. Pneumoconioses (e.g. asbestosis, silicosis)
    b. Post-infectious ILD
    c. Iatrogenic ILD caused by drugs and/or radiation
    d. Extrinsic allergic alveolitis (hypersensitivity pneumonitis)
    e. ILD in Rheumatoid arthritis
    f. ILD in SLE
2. Those of idiopathic causes;
    a. Sarcoidosis
    b. Idiopathic interstitial Pneumonias e.g.non specific interstitial pneumonia, acute interstitial pneumonia, desquamative interstitial pneumonia, respiratory bronchiolitis

Signs and symptoms

The symptoms of ILDs appear gradually and they may not be apparent until the disease is fully established. The progression varies from person to person and the disease affects people differently. The symptoms vary from moderate to severe. Some of the symptoms include;

Signs of Symptoms of ILDs

- Shortness of breath especially on exertion
- Chronic dry or hacking cough
- Weight loss
- Finger and toe clubbing
- Unusual tiredness that persists for long
- Decreased exercise tolerance
- Cyanosis in severe cases
- Characteristic inspiratory crackles on auscultation due to fibrosis

Differential diagnosis of ILDs

- Asthma
- Tuberculosis
- Chronic Obstructive Pulmonary Disease (COPD)
- Congestive heart failure
- ILDS can coexist with all the above and other diseases

Diagnostic test

- Chest X Ray and chest CT scan which show signs of scarring/fibrosis. Interstitial lung markings, small lungs.
- Pulmonary function tests- Spirometry to measure the lung capacity.
- Blood test depending on suspected cause. E.g. autoimmune antibodies against common allergens.
- Lung biopsy –bronchoscopy.

Management of ILDs

Regardless the cause of ILD, the goals of treatment are:

- To decrease inflammation and prevent further lung scarring
- Where possible, to remove source of the problem
- To reduce and manage complications of ILD
- To improve patient's health status and quality of life

A. Pharmacotherapy/ medications

Many drugs are used to treat interstitial lung diseases. The role of the medications is to;

- Improve breathing.
- Reduce tissue inflammation.
- Suppress hyperactive immune systems.

Management of ILDs includes;

- Some types of ILDs respond to corticosteroids and/or immunosuppressants by slowing down inflammation which leads to scarring
- If the ILD is due to exposure to drugs or allergen, then stop the drug or avoid the allergen
- Oxygen therapy
- Lung transplant
- In severe breathlessness- pulmonary physiotherapy and oxygen therapy
- Non pharmacological management
- Nutritional modification
- Stop smoking
- Exercise
- Avoid/ control infections
- Avoid allergens and dusts.

G) Lung Cancer

Cancer of the lungs is an important differential diagnosis in patients with chronic respiratory symptoms. Cancers in the lungs can be either primary or secondary. The most common primary lung cancer is Non- small cell type (NSCLC) accounting for 80% of all cases. This results from smoking and rarely affects non-smokers. (*Ref. National guidelines for cancer management, August 2013)*

Diagnosis

1. Clinical symptoms

Lung cancer does not usually cause symptoms in its early stages. About 20% of those diagnosed with Lung cancer are identified incidentally while seeking health care for other conditions.

Clinical symptoms of lung cancer	
• Chronic cough with or without haemoptysis • changes in a 'smoker's' cough • Chest pain • Wheezing	• Shortness of breath • Hoarseness of voice • Unexplained weight loss • Fatigue • Dysphagia

NB: Symptoms due to spread depend on the organ involved.

2. **Imaging**

This involves:

a. Chest radiography - Most will show features of mass or enlarged lymph nodes. Others include multiple nodes with cavitations due to necrosis of centrally located malignant tissue, mediastinal mass, features of consolidation

b. CT scan. This provides more details and also assist in staging of the disease

c. Others: MRI, Positron Emission Tomography (PET)

3. Tissue diagnosis of biopsy (obtained through bronchoscopy, mediastinoscopy, open biopsy etc), FNA cytology. Sputum or thoracocentesis specimens can be obtained for cytology.

Management of Lung cancer

Early detection is key in cancer management and reduction in mortality.
The aim of management is to;

- Cure patients in early stages
- Reduce disease progression
- Relieve symptoms
- Palliative care for advanced disease

The management of lung cancer is multidisciplinary. For detailed management plan for Lung cancer, *refer to the National guidelines for cancer management in Kenya*

H) Tobacco Smoking Cessation

Tobacco smoking is a chronic addiction that usually requires repeated interventions over a long period of time. The aim of managing the addiction is to ensure long term or permanent abstinence

Smoking cessation is the one single most intervention with the greatest capacity to influence onset and progression of some lung diseases including COPD and asthma. In 2003, the prevalence of tobacco smoking in Kenya was 23% for males and 3% for females. WHO estimated that 6.4 billion sticks of cigarettes were smoked that year. In 2008 the prevalence was estimated at 19% for males and 2% for females with the former Central province leading with 30%, Eastern 26%, Coast 22.6%, Nairobi 17.1%, N. Eastern 15.6%, Rift Valley 14.3%, Western 11.2% and Nyanza 7.9%. These figures are for males only since most females do not disclose their tobacco use status due to social cultural inhibitions {ref. National tobacco control action plan -2010 -2015}.

The recommended smoking cessation framework includes a mix of three main strategies:

1. A public health approach that seeks to change the social climate and promote a supportive environment.

2. A health systems approach that focuses on promoting and integrating clinical best practices (behavioral and pharmacological) which help tobacco-dependent consumers increase their chance of quitting successfully.
3. A surveillance, research and information approach that promotes the exchange of information and knowledge so as to increase awareness of the need to change social norms.

The Public health approach

Kenya became a party to the WHO Framework Convention on Tobacco Control on February 2005 (Source: Kenya Tobacco control laws). A national Tobacco control plan has been developed and there are also laws on Tobacco use, advertising and promotion. The goal of the Tobacco control plan is to reduce the prevalence of tobacco use, its associated diseases, disability and deaths in Kenya.

National law on Tobacco smoking

Smoke free places: Smoking is allowed in designated smoking areas in most public places and workplaces.
Tobacco adverting, Promotion and sponsorship: The law prohibits virtually all forms of advertising and promotion of tobacco products.

Tobacco packaging and labeling: Rotating, text only health warnings must cover 30% of the front and 50% of the back of the package and must be displayed in English and Kiswahili.

(Details in the 'Tobacco control Act 2007 CAP 245)

Health care workers can contribute to this plan through;

1. Helping users to quit by
    a. Campaigns during World no tobacco day
    b. Advice to quit smoking during hospital visits
    c. Offering cessation services (detailed below) and intensive support
    d. Create awareness among community on the availability of cessation services
    e. A referral mechanism for tobacco cessation from community
2. Helping to protect non- smokers from the effects of second hand smoke (SHS)
   The aim is to protect the general public especially children from tobacco smoke. This includes advocating for and promoting smoke-free environments (households, workplaces and public places).

   Health care workers can help by:-
   a. Raising awareness of adolescents, pregnant women and children on the dangers of second hand smoke
   b. Advocating for smoke free policies in their workplaces

Health System Approach

Tobacco use cessation is one of the most important measures to reducing smoking- caused deaths and disease. Quitting smoking at any age results in immediate health benefits, irrespective of how long a person has been smoking.

How to treat your patient's tobacco addiction: Ask every patient who comes to the clinic: Do you smoke or have you ever smoked? Record in the patient's record form/card their smoking status – **smoker, never-smoked, ex-smoker.**

Brief strategies to help patient willing to quit smoking: (*Global strategy for the diagnosis and prevention of COPD- 2015*)

Ask: Systematically identify all tobacco users at every visit. Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco use status is queried and documented

Advise: Strongly urge all tobacco users to quit. In a clear, strong, and personalized manner, urge every tobacco user to quit

Asses: Determine willingness to make a quit attempt. Ask every tobacco user if he/she is willing to make a quit attempt at this time (e.g. within the next 30 days)

Assist: Aid the patient in quitting. Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support, help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials

Arrange: Schedule follow-up contact. Schedule follow-up contact, either in person or via telephone

Strategies to help those not yet ready to quit smoking

The objective is to help the patient reflect on his/her smoking and desire to quit

- Ask the patient about and discuss the impact of smoking on the patient's life
- Link every smoking- related illness in the patient to his/her smoking
- Provide a strong personalized message
- Encourage patient to make his/her house and car smoke free
- Provide educational materials (if any)

To increase patient's motivation to quit;

- Offer to help your patient
- Ask about your patient's concerns about quitting and discuss ways of dealing with them
- Give patient educational materials
- Suggest a follow-up visit

Smoking cessation for adolescents

The effect of tobacco smoking are long term and therefore difficult to convince adolescents to stop smoking. There is insufficient evidence to inform recommendations among this population. However, one can use reasons that may have an effect on this age group, such as explaining that smoking causes wrinkles, bad breath, yellow teeth etc.

Tobacco smoking strategies

Once a smoker is ready to quit, you can choose the right intervention by assessing the level of nicotine dependence, quit history and co-morbidity.

Assessment	Intervention
• No co-morbidity • Low nicotine dependence (<20 cigarettes/ day) • No past serious quit attempts	• Self-help strategies
• No co-morbidity • Low nicotine dependence and several past serious quit attempts OR high nicotine dependence (> 20 cigarettes per day and smoking within 30 mins of waking up) and no past serious quit attempt	• Brief, tailored counseling with follow up
• Co-morbidity • Low nicotine dependence and past serious quit attempts OR high nicotine dependence with at least one past serious quit attempt.	• Specialized intensive treatment

Medical management of tobacco addiction

Nicotine is the chemical component in tobacco that causes dependence and the nicotine withdrawal symptoms, Nicotine dependence develops fairly rapidly- often within 6 months of regular use. The severity of dependence depends more on the difficulty the patient has in quitting smoking than on the amount of tobacco smoking. Nicotine withdrawal syndrome occurs when blood nicotine levels fall sharply but can also be triggered by presence of other psychoactive substances e.g. alcohol and/or environmental stimuli. Nicotine withdrawal is usually greater in the high nicotine dependence individuals.

Signs of nicotine withdrawal syndrome

- Dysphoric or depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating, restlessness
- Decreased heart rate
- Increased appetite or weight gain

Treatment of nicotine dependence and withdrawal syndrome

- Nicotine replacement therapy (NRT) and/or Bupriopion regularly or episodically
    - Nicotine gum – 'bite & park' 1 piece of gum every 1-2 hours for several weeks to months or longer if necessary. Stop smoking before starting treatment
    - Nicotine patch – For light smokers (<20 sticks/ day) start 14 or 7mg and for heavy smokers (> 20 sticks/day) start 21mg for 4-8 weeks tapering to lower doses as the dependence reduces
    - Nicotine inhaler
    - Nicotine nasal spray
    - Bupriopione -150mg 4 times /day for 3 days then twice/ day for 7-12 weeks or longer if necessary. Start 7-14 days before quit date
    - Antidepressant
- Withdraw NRT once the individual is more comfortable with environmental triggers and emotional states associated with his/her tobacco addiction
- Discuss with the patient behavior associated with tobacco addiction e.g. 'handling the cigarette, the feel of smoke in one's mouth or throat etc and work out lifestyle modification measures
- Dependence on other psychoactive substances (e.g. alcohol, cannabis etc) makes recovery from tobacco addiction more difficult

CHAPTER 3

TUBERCULOSIS

A. Background and Introduction to Tuberculosis

Introduction to Tuberculosis

Aetiology

TB is an airborne disease caused by the bacterium Mycobacterium tuberculosis (M. tuberculosis). M. tuberculosis and seven very closely related mycobacterial species (M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti and M. mungi) together comprise what is known as the M. tuberculosis complex. Most, but not all, of these species have been found to cause disease in humans. The majority of TB cases are caused by M. tuberculosis. M. tuberculosis organisms are also called tubercle bacilli.

In rare situations Mycobacteria other than Tuberculosis (NTM) may cause a disease similar to typical TB. Infection with M. tuberculosis usually results from inhalation of infected droplets produced by a patient who has pulmonary TB. The source of infection for most children is an infectious adult in their close environment (usually the household). This exposure leads to the development of a primary parenchymal lesion (Ghon focus) in the lung with spread to the regional lymph nodes. MTB usually infects the lungs, but TB bacteria can infect any part of the body such as the kidney, spine, and brain. If not treated properly, TB disease can be fatal.

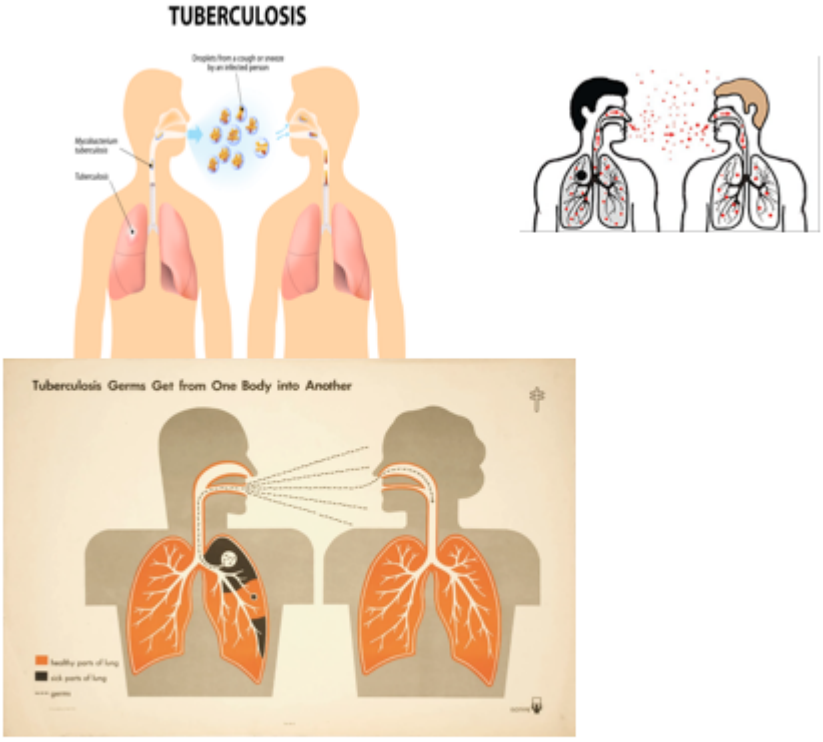
The immune response (a delayed hypersensitivity and cellular immunity) develops about 4 -6 weeks after the primary infection. In most cases, the immune response stops the multiplication of M. tuberculosis bacilli at this stage. However, a few dormant bacilli may persist. A positive tuberculin skin test (TST) or Interferon Gamma Release Assay (IGRA) where available would be the only evidence of infection.

In some cases, the immune response is not strong enough to contain the infection and disease occurs within a few months. The risk of progression to disease and development of disseminated TB is increased in the very young (0-4 years), immune-compromised and malnourished children. In the vast majority of children who develop disease, they usually do so within 2 years following exposure and infection. Children can present with TB at any age, but the most common age is between 1 and 4 years.

Transmission

M. tuberculosis is carried in airborne particles, called droplet nuclei, of 1– 5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. These tiny particles can remain suspended in the air for several hours. M. tuberculosis is transmitted through the air, not by surface contact. Transmission occurs when a person inhales droplet nuclei containing M. tuberculosis, and the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs.

Figure 3.1: Transmission of Tuberculosis



TB is spread through the air from one person to another through droplet nuclei (<5 microns) each containing 1-5 bacilli. The MTB infected droplet nuclei are released into the air when a person with TB disease of the lungs or throat coughs, sneezes, speaks, or sings. Droplet nuclei may also be produced by aerosol-producing investigations such as sputum induction, bronchoscopy and through manipulation of lesions or processing of tissue or secretions in the laboratory. They can

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Natural History of Tb Infection

Definitions

Latent TB infection is when a person carries the Mycobacterium tuberculosis bacteria inside the body. Many people have TB infection and are well. A positive TST indicates infection but a negative TST does not exclude the possibility of infection.

Active TB disease occurs in someone with TB infection when the bacteria inside the body start to multiply and become numerous enough to damage one or more organs of the body. This damage causes clinical symptoms and signs and is referred to as "tuberculosis" or active disease.

Index Case: Usually an adult with smear positive pulmonary TB.

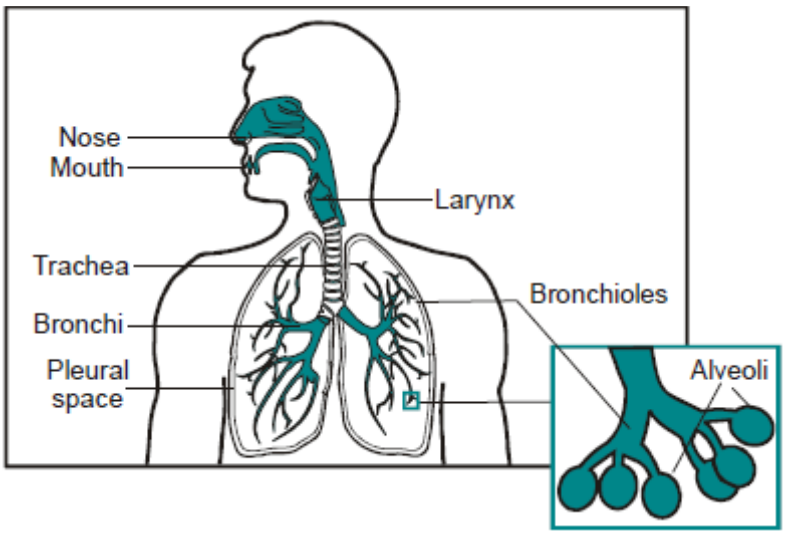
Close/TB contact is defined as living in the same household as, or in frequent contact with (e.g. child minder, school staff) an index case with PTB.

A child refers to the 0 to 14 year age group.

An Infant is a child of less than 1 year of age (0-12 month age group).

When a person inhales air that contains droplets with M. tuberculosis bacilli, most of the larger droplets become lodged in the upper respiratory tract (the nose and throat). However, smaller droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection may begin.

Figure 3.2: The Lungs and the alveoli



In the alveoli, some of the tubercle bacilli are killed, but a few multiply in the alveoli and enter the bloodstream and spread throughout the body. Bacilli may reach any part of the body. Within 2 to 8 weeks, however, the body's immune system usually intervenes, halting multiplication and preventing further spread. The immune system is the system of cells and tissues in the body that protect the body from foreign substances. At this point, the person has latent TB infection (LTBI). 70-90% of persons exposed to TB bacilli do not develop any infection whereas 10-30% develops infection.

Latent TB Infection (LTBI)

Latent TB infection (LTBI) means that tubercle bacilli are in the body, but the body's immune system is keeping the bacilli under control and inactive. The immune cells form a shell that acts as a fence and keeps the bacilli contained and inactive. People who have LTBI but not TB disease are NOT infectious — in other words, they cannot spread the infection to other people. These people usually have a normal chest x-ray. LTBI is not considered a case of TB.

TB Disease (Active TB disease)

Some people with LTBI develop TB disease. TB disease develops when the immune system cannot keep the tubercle bacilli under control and the bacilli begin to multiply rapidly. The risk that TB disease will develop is higher for some people than for others e.g. children 0-4 years of age and immune-compromised persons i.e. those with HIV, severe malnutrition, Diabetes, on chemotherapy etc. TB disease can develop very soon after infection or many years after infection.

Unless treated, about 5% of the people who have recently been infected with M. tuberculosis will develop TB disease in the first year or two after infection. Another 5% will develop TB disease later in their lives. In other words, about 10% of all people with normal immune systems who have LTBI will develop TB disease at some point in their lives. The remaining 90% will stay infected, but free of disease, for the rest of their lives.

Major similarities and differences between LTBI and Active TB disease are shown below:

LTBI vs. TB Disease

Latent TB Infection (LTBI)	TB Disease (in the lungs)
Inactive tubercle bacilli in the body	**Active** tubercle bacilli in the body
Tuberculin skin test or QuantiFERON®-TB Gold test results usually positive	Tuberculin skin test or QuantiFERON®-TB Gold test results usually positive
Chest x-ray usually **normal**	Chest x-ray usually **abnormal**
Sputum smears and cultures **negative**	Sputum smears and cultures may be **positive**
No symptoms	**Symptoms** such as cough, fever, weight loss
Not infectious	**Often infectious** before treatment
Not a case of TB	**A case of TB**

Prognosis of TB

If left untreated, active pulmonary TB naturally progresses with the following outcomes within 5 years: 50% of the cases die, 25% are spontaneously cured while 25% remain chronic coughers. Proper treatment with anti-TB medicines leads to a cure and reduces mortality to less than 5%.

Figure 3.3: Exposure of TB and Progression

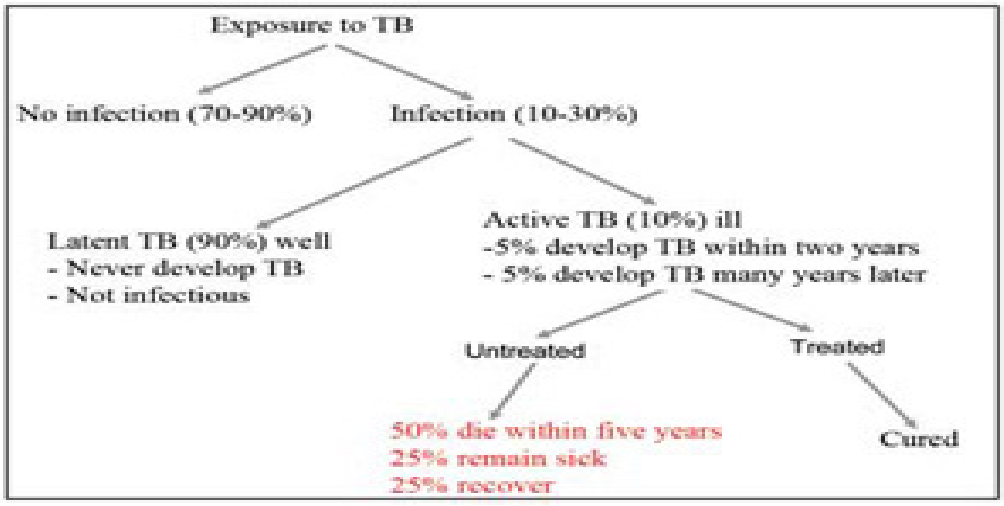


Table 3.1: Risk factors for LTBI (TB infection) and progression from infection to Active TB disease

Risk factors for TB infection (exposure) (LTBI)	Risk factors for active TB disease
High prevalence of TB disease in population	Immunosuppression e.g HIV, diabetes, Malnutrition, alcoholism, smoking, immunosuppressant therapy, silicosis
Smear positivity of cases in population (infectivity of cases)	Recent prior infection
Type of TB disease (e.g cavitary, pulmonary more infectious)	Poorly treated previous TB
Proximity and duration to infectious cases (contact)	Extremes of age
Environmental factors e.g. poor ventilation, overcrowding	

To note:

HIV infection- Infection with HIV increases the risk of progression of recent M. tuberculosis infection and of reactivation of latent M. tuberculosis infection by 5–15% annually whereas it is 10% over a lifetime for people infected only with M. tuberculosis. HIV also increases the rate of relapse and re-infection.

Diabetes- diabetes triples the risk of developing TB among people with diabetes than in the general population.

Time since infection (Recent infection) - During the first 2 years after infection, people with TB infection are at high risk of developing TB disease. 50% of children below 1 year of age progress to active TB disease within the first year of being infected with TB.

Gender (males more than females) - Because of poor health seeking behavior among males coupled with their social habits.

Silicosis- Silicosis, is the most prevalent of the pneumoconioses, and is caused by inhalation of crystalline silica particles through exposure from mining, quarrying, tunneling, and working with metal ores. Silica is a main part of sand, so glass workers and sand-blasters are also exposed to silica.

Silica-exposed workers, with or without silicosis, are at increased risk for tuberculosis and non-tuberculous mycobacteria-related diseases (NTM).

Alchoholism- The risk of active tuberculosis is substantially elevated in alcoholics. This may be due to the increased risk of infection related to specific social mixing patterns associated with alcohol use, as well as the influence of alcohol and of alcohol related conditions on the immune system itself.

Classification of TB

This section describes the revised definitions of TB cases, their classification and the treatment outcome categories.

A presumptive TB case is one who presents with symptoms or signs suggestive of TB (previously known as a TB suspect).

Case definitions

a) **A bacteriologically confirmed TB case:** one from whom a biological specimen is positive by smear microscopy, culture or WRD (WHO-approved rapid diagnostics such as Xpert MTB/RIF). All such cases should be notified regardless of whether TB treatment was started or not.

b) **A clinically diagnosed TB case**; 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 extrapulmonary 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

Table 3.2: Classification of TB

1. Classification based on anatomical sites	
Pulmonary TB(PTB)	Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. This exclude pleural effusion
Extra pulmonary TB (EPTB)	Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lung parenchyma, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.
2. Classification based on history of previous TB treatment (patient registration group)	
New patients	Patient who has never been treated for TB or has taken anti-TB drugs for less than 1 month.
Previously treated patients	Patient who has 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: **a) Relapse patients;** previously treated for TB, 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 reinfection). **b) Treatment after failure patients;** previously treated for TB and whose treatment failed at the end of their most recent course of treatment. **c) Treatment after loss to follow-up patients;** previously treated for TB, and declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as return after default patients).
Patients with unknown previous TB treatment history do not fit into any of the categories listed above	
3. Classification based on HIV status	
HIV-positive TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV testing conducted at the time of TB diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in the pre-ART register or in the ART register once ART has been started.
HIV-negative TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has a negative result from HIV testing conducted at the time of TB diagnosis. Any HIV-negative TB patient subsequently found to be HIV-positive should be reclassified accordingly.
HIV status unknown TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing and no other documented evidence of enrolment in HIV care. If the patient's HIV status is subsequently determined, he or she should be reclassified accordingly.

4. Classification based on drug resistance, based on Drug susceptibility testing	
Monoresistance	Resistance to one first-line anti-TB drug only.
Polydrug resistance	Resistance to more than one first-line anti-TB drug (other than both isoniazid and rifampicin).
Multidrug resistance	Resistance to at least both isoniazid and rifampicin
Extensive drug resistance	Resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance
Rifampicin resistance	Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether monoresistance, multidrug resistance, polydrug resistance or extensive drug resistance.

Please note:

1. All TB patients must be tested for HIV, and all efforts must be made to classify them either as HIV positive or HIV negative as this impacts management.
2. The above categories of classification based on drug resistance are not all mutually exclusive. When enumerating rifampicin-resistant TB (RR-TB), for instance, multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are also included.

Treatment outcome definitions

The new treatment outcome definitions make a clear distinction between two types of patients:

i) Patients treated for drug-susceptible TB.

ii) Patients treated for drug-resistant TB using second-line treatment (defined as combination chemotherapy for drug-resistant tuberculosis which includes drugs other than those in Group 1).

The two groups are mutually exclusive. Any patient found to have drug-resistant TB and placed on secondline treatment is removed from the drug-susceptible TB outcome cohort. This means that management of the standard TB register and of the second-line TB treatment register needs to be coordinated to ensure proper accounting of the outcomes of treatment.

Treatment outcomes for Drug sensitive TB patients

All bacteriologically confirmed and clinically diagnosed TB cases who are sensitive to 1st line drugs should be assigned an outcome from this list.

Table 3.3: Treatment Outcomes for Drug Sensitive TB Patients

Outcome	Definition
Cured	A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
Treatment success	The sum of cured and treatment completed. This is calculated based on bacteriologically confirmed cases.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.

Outcomes for RR-TB/MDR-TB/DR TB/XDR-TB patients treated using second-line treatment Patients found to have an RR-TB or DR-TB TB strain at any point in time should be started on an adequate second-line drug regimen. If treatment with a second-line drug regimen is not possible, the patient is kept in the main TB cohort and assigned an outcome from among those in the table above.

Table 3.4: Treatment Outcomes for RR-TB/MDR-TB/DR TB/XDR-TB patients treated using second-line treatment

Outcome	Definition
Cured	Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.
Treatment completed	Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

Treatment success	The sum of cured and treatment completed
Treatment failed	Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of: • lack of conversion by the end of the intensive phase(8 months) • or bacteriological reversion in the continuation phase after conversionb to negative, • or evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, • or adverse drug reactions (ADRs).
Died	A patient who dies for any reason during the course of treatment.
Lost to follow-up	A patient whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A patient for whom no treatment outcome is assigned. (This includes cases "transferred out" to another treatment unit and whose treatment outcome is unknown)
Key definitions in DR TB management	
Conversion (to negative	culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion.
Reversion (to positive)	culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining Treatment failed, reversion is considered only when it occurs in the continuation phase.

Control of Tuberculosis

The End TB Strategy

The previous STOP TB STRATEGY that drew to a close in 2015 had various notable achievements. Among these was 37 million lives saved between the year 2000 and 2013 through effective TB diagnosis and treatment, a 45% decline in TB mortality rate, a 41% decline in TB prevalence rate since 1990, HIV related TB deaths reduced by 34% in the last decade with triple the number of DR TB cases diagnosed and a three-fold increase in treatment coverage since 2009. However there were 3 million people with TB missed by the health systems every year with TB/HIV interventions still in need of further scaling up with a widening gap between people diagnosed with MDR-TB and those put on treatment. This could compromise the gains made in MDR TB management.

In the interest of social justice and universal health coverage, everyone with TB should have access to tools and services for rapid diagnosis, treatment and care which is the cornerstone of the end TB strategy as outlined in Figure 3.4.

Figure 3.4: The End TB Strategy

VISION	**A world free of tuberculosis – zero deaths, disease and suffering due to tuberculosis**			
GOAL	**End the global tuberculosis epidemic**			
INDICATORS	**MILESTONES**		**TARGETS**	
	2020	**2025**	**SDG 2030***	**END TB 2035**
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	80% (<20/100 000)	90% (<10/100 000)
TB-affected families facing catastrophic costs due to TB (%)	Zero	Zero	Zero	Zero

PRINCIPLES

1. *Government stewardship and accountability, with monitoring and evaluation*
2. *Strong coalition with civil society organizations and communities*
3. *Protection and promotion of human rights, ethics and equity*
4. *Adaptation of the strategy and targets at country level, with global collaboration*

PILLARS AND COMPONENTS

1. **INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION**
   - A. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
   - B. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
   - C. Collaborative tuberculosis/HIV activities, and management of co-morbidities
   - D. Preventive treatment of persons at high risk, and vaccination against tuberculosis
2. **BOLD POLICIES AND SUPPORTIVE SYSTEMS**
   - A. Political commitment with adequate resources for tuberculosis care and prevention
   - B. Engagement of communities, civil society organizations, and public and private care providers
   - C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
   - D. Social protection, poverty alleviation and actions on other determinants of tuberculosis
3. **INTENSIFIED RESEARCH AND INNOVATION**
   - A. Discovery, development and rapid uptake of new tools, interventions and strategies
   - B. Research to optimize implementation and impact, and promote innovations

Global priority indicators and targets for monitoring the implementation of the End TB Strategy

All countries should aim to reach these targets at the latest by 2025.

- Treatment coverage Number of people that developed TB, and were notified and treated, out of the total estimated number of incident cases in the same year (%): **≥ 90%**
- TB treatment success rate Number of TB patients who were successfully treated out of all notified TB cases (%): **≥ 90%**
- Preventive treatment coverage Number of people living with HIV and children who are contacts of cases who were started on preventive treatment for latent TB infection, out of all those eligible (%): **≥ 90%**
- TB affected households facing catastrophic costs Number of TB patients and their households that experienced catastrophic costs due to TB, out of all TB patients (%): **0%**
- Uptake of new diagnostics and new drugs Number of TB patients who were diagnosed using WHO-recommended rapid tests, out of all TB patients (%): **≥ 90%**
- Number of TB patients who were treated with regimens including new TB drugs, out of those eligible for treatment with such drugs (%): **≥ 90%**

Role of The National Tuberculosis, Leprosy and Lung Disease Program (NTLD-P)

NTLD-P is a program in the Department of Disease Prevention and Control under the Ministry of Health (MoH). It is charged with the overall coordination of control of TB, Leprosy and Lung Disease. Its mandate is to coordinate the development of policy guidelines, setting of standards, resource mobilization, ensuring an uninterrupted supply of commodities, provision of supportive supervision and coordination, monitoring and evaluation in line with international and local strategies.

This mandate is executed in collaboration with partners involved in TB, Leprosy and Lung Disease control. The control activities are coordinated by County TB and Leprosy Coordinators (CTLCs) and sub county TB and Leprosy Coordinators (sCTLCs) at the county and sub county levels respectively. The TB and Leprosy coordinators are integral members of the Health Management Teams at various levels. The delivery of DOTS services is integrated into the general health services provided at health care delivery points. By the end of 2014 TB services were available in 3,220 public, NGO and private health care facilities which provide TB treatment services. TB smear microscopy is available in 1,920 laboratories country wide.

NTLD-P organogram denoting facility, sub county, county and national level flow of TB adminstrative information and data.

Diagnosis of Tuberculosis

Drug Sensitive TB

The diagnosis of TB depends on numerous factors from the patient themselves, the community as a whole and the health facility. These factors include:

i) High index of TB suspicion among community members.

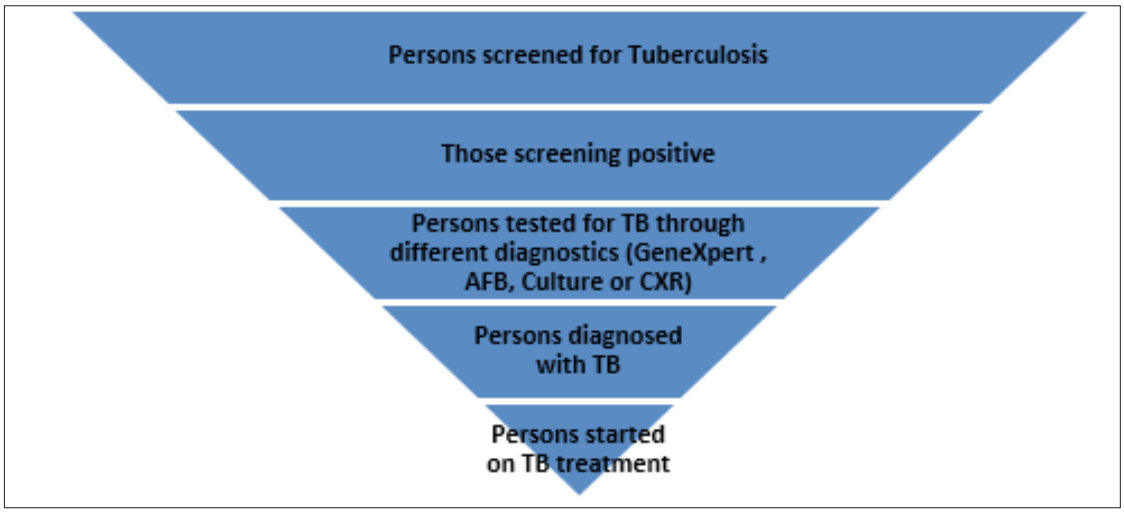
ii) High index of suspicion among health care workers

iii) Turnaround time for delivery of laboratory results

iv) Capacity to conduct active tracing and screening of contacts, to follow up all patients with positive lab investigations (bacteriologically confirmed) for timely treatment initiation.

v) Integration of TB services within other areas such as maternal and neonatal child health, nutrition, diabetes and HIV clinics

Figure 3.5: Cascade of Intensive Case Finding to Increase Case Detection of Tuberculosis



B. Diagnosis of Pulmonary Tuberculosis (PTB)

Diagnosis of Pulmonary TB (PTB)

Diagnosis of PTB begins with a high index of suspicion based on history and physical examination. Investigations are therefore done to confirm a diagnosis.

i) History

History of presenting complaints

TB should be suspected in any person presenting with the following;

- cough
- fevers
- night sweats
- loss of weight
- chest pain
- shortness of breath

History of contact with an adolescent or adult with proven or suspected TB should be taken for all children suspected to have TB.

ii) Physical examination

Physical signs may include:

- Bronchial breath sounds
- Tachypnoea
- Wasting
- Haemoptysis
- Anaemia

In children there may be atypical clinical presentations, such as the following;

a) Acute severe pneumonia

- Presents with fast breathing and chest in-drawing
- Occurs especially in infants and HIV-infected children

Suspect PTB if response to antibiotic therapy is poor. If HIV infected also suspect other HIV-related lung disease e.g. PCP.

b) Wheeze

Asymmetrical/persistent wheeze in spite of broncho-dilators (airway compression due to enlarged tuberculous hilar lymph nodes).

iii) Investigations

Table 3.5: TB Investigations

Laboratory test	Target	Purpose
1. GeneXpert	The first line test for all presumptive TB in; • children, • PLHIV • HCWs • prisoners, • smear negative persons • previously treatment TB	For diagnosis of TB
2.Smear microscopy (Fluorescent and Light microscopy)	All presumptive Pulmonary TB	Detect TB disease Monitoring smear positive and gene xpert positive TB patients on treatment at months 2, 5 and 6
3. Chest X-ray	All presumptive pulmonary TB	Support TB diagnosis especially where sputum for AFB/gene xpert is negative.
4. Histology	All presumptive EPTB	Tissue diagnosis in suspected EPTB e.g TB adenitis

Other supportive tests		
Tuberculin skin test	Children	As an adjunct test to detect TB exposure in children, whose TB diagnosis is not obvious. Conducted in tertiary institutions
ESR	In presumptive TB	Erythrosite Sedimentation Rate (ESR) is usually elevated in active TB, but this test is not sensitive or specific enough to be of value in the diagnosis of PTB.
All attempts must be made to make a bacteriological diagnosis of PTB in both adults and children. Sputum for AFB or Gene Xpert is therefore mandatory for all presumptive cases of PTB.		

Sputum smear examination

TB diagnosis using sputum for ZN and FM microscopy involves collection of 2 sputum samples, a spot and a morning sample as follows;

Table 3.6: Spot and morning sputum collection strategy

Sample	When is it collected?	Where is it collected?
Spot - 1st sample	On the spot when patient presents to facility	In the health facility
Morning - 2nd sample	Patient collects upon waking up the following morning	At home and brings to health facility (Or in hospital if patient is hospitalized)

Instructing patients to collect sputum specimen

The patient should do the following for quality sputum sample;

1. Take a deep breath.
2. Cough severally.
3. Attempt sputum production. Number 1 to 3 can be repeated several times.
4. Spit sputum (and not saliva) into the provided container.
5. Close the lid tightly.
6. Submit to laboratory as soon as possible.

Instructions for HCWs who collect patient samples for evaluation

1. Label the sputum containers on the side (not on the lid) prior to sputum collection.
2. Fill in the sputum examination forms ensuring that the patient's contacts are included.

3. Instruct the patient to collect sputum samples in a well ventilated area preferably outdoors (not in the facility lavatories).
4. Give patients clear instructions on when to return for their results.

Results should ideally be available within 24 hours after the sample is submitted.

In patients who cannot expecorate, sputum may be obtained through:

1. Gastric aspiration; Through insertion of a nasogastric tube (NGT) to aspirate gastric contents
2. Sputum induction done through nebulization with hypertonic saline (greater 0.9%) solution, followed by
3. Bronchial wash or broncho-alveolar lavage sample obtained through fiberoptic bronchoscopy

NB. Sputum induction and bronchoscopy may lead to a substantial generation of infectious aerosols, and should only be carried out in clinical environments with appropriate infection prevention measures in place.

Sputum culture examination

In general the indications for sputum TB culture and DST are:

- All previously treated patients(including relapse, treatment after failure, treatment after loss to follow up and other previously treated patients)
- Patients who remain smear positive at end of month 2 while on first line treatment
- Patients with treatment failure (Smears still remains positive at month 5 or later during treatment)
- Symptomatic contacts of drug resistant TB cases
- Health care workers

Gene Xpert

This is a molecurar test to detect prescence of *M. Tuberculosis* as well as Rifampicin resistance. It is more sensitive and specific than sputum micsroscopy in detecting TB. It is the preferred test of choice for TB dignosis among children, PLHIV, HCWs, prisoners, smear negative persons and previously treated persons. The test takes 2 hours thus reducing the time taken to diagnose TB and detect Rifampicin resistance. This increases case detection of TB and reduces transmission.

Chest X-ray

The chest x-ray may aid the diagnosis of PTB but it should not be used as the sole means of establishing a TB diagnosis.

All patients with chest x-ray features suggestive of TB should have sputum specimens submitted for microbiological examination. It is a major omission to diagnose TB on the basis of a chest x-ray ONLY

The radiographic features that may be suggestive of PTB include:

- Upper zone of lung showing patchy shadows (May have evidence of cavitations and scarring (fibrosis)
- In HIV infected persons the radiological picture is more often atypical with the lower or mid-zone shadows and the presence of hilar or mediastinal lymph node enlargement being relatively common.
- Miliary NTMling, Pleural and/or pericardial effusion (Case of EPTB).

Differential Diagnosis Put After Diagnosis

- Chronic bronchitis/ COPD
- Bronchiectasis
- Lung abscess,
- Lung cancer
- Heart failure
- Sarcoidosis
- Atypical pneumonias e.g. (caused by unusual pathogens such as fungi including *pneumocytis jirovecii*)

Complications of PTB

i. Spontaneous Pneumothorax

It is the prescence of air in the pleural cavity resulting to impairment of oxygenation and ventilation. It is a medical emergency and results from rupture of a TB cavity adjacent to the pleura. It may be associated with formation of pus in the pleural space (empyema) leading to a pyopneumothorax.

Presentation:

- Acute onset shortness of breath
- Chest pain.

Management:

- The patient should be admitted to hospital for appropriate management.
- Underwater seal drainage

ii. Bronchiectasis

This is a chronic lung disease often secondary to an infectious process that results in the abnormal and permanent distortion of one or more of the conducting brochi or airways.

Presentation

- Cough
- Copious amounts of sputum which is mainly greenish, blood stained and foul smelling.
- Hemoptysis.

Management

- The hallmark of management of productive bronchiectasis is chest physiotherapy. This includes postural drainage and other manoeuvres aimed at improving drainage of respiratory secretions.
- Infective exacerbations will require antibiotics. Broad spectrum antibiotics like amoxycillin-clavulanate, Metronidazole or clindamycin for anaerobic infection. Antipseudomonal antibiotic like ciprofloxacin, 3rd generation cephalosporin (Ceftazidime) should be used when colonization with *Pseudomonas* is suspected.
- If hemoptysis is severe and life threatening, patients should be admitted to hospital for more specialized treatment.

iii. Fibrosis of the lungs

- This is sequelae of extensive tuberculous disease.
- In severe terminal cases, long term oxygen therapy may be required.
- These patients should be referred for review and specialised care by a physician.

iv. Lung abscess

- Seen in a patient with extensive damage to the lungs after tuberculosis.
- Antibiotic treatment is given. The choice of antibiotic is aided by the results of a pus culture-sensitivity test.
- Surgical intervention may also be necessary.

v. Aspergilloma

Result of colonization of tuberculous cavities or bronchiectatic lesions with the fungus A*spergilus.*

Presentation

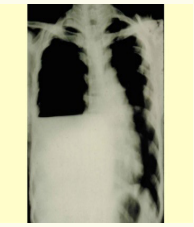
- Recurrent or persistent haemoptysis patient previously treated for TB.
- Malaise
- Fever
- Chest x-ray shows a cavity with an air crescent (halo) around it
- High levels of specific immunoglobulin G against Aspergillus in blood (Confirmatory test).

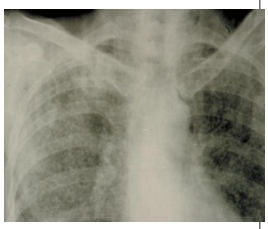
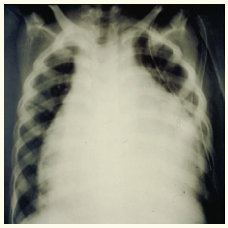
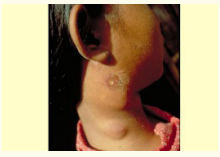
The only effective treatment is surgical removal of the aspergilloma.

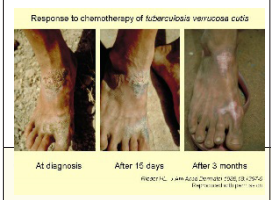
C. Diagnosis of Extra-Pulmonary TB

Common Forms of Extra-Pulmonary TB and Diagnostic Approaches

Table 3.7: Common Forms of Extra-Pulmonary TB- Signs Symptoms and Diagnostic Approaches

Form of Extra-Pulmonary TB	Signs and Symptoms	Diagnosis
Plueral TB with Pleueral Effusion 	Tuberculous pleural effusion usually presents with: Local chest symptoms that include chest pain. Shortness of breathlessness whose degree depend on amount of effusion. Many patients also have a cough and systemic symptoms including fever and night sweats. When examined the trachea and the point of maximum cardiac impulse (apex beat) may be found to have shifted away from the side of the effusion. Percussion of the chest reveals "stony" dullness and breath sounds are reduced on the side of the effusion.	Chest x-ray is often required to confirm the presence of the effusion especially when effusion is small. It is also advisable, if the expertise exists, to always perform a diagnostic pleural aspiration at the minimum to distinguish pus (emphysema) from "usual" effusion. Where facilities exist aspirated fluid should be sent to the laboratory for biochemical tests (sugar, protein, and lactic dehydrogenase), cell count, cytology and microbiological tests including smears for tubercle bacilli. A pleural biopsy is rarely required in young patients below the age of 40 years. Older patients and especially those with a significant smoking history may have other diagnoses and in these patients it is advisable to perform a pleural biopsy using an Abrahm's needle.
Tuberculosus Peritonitis and Ascites	Tuberculosus Peritonitis and Ascites usually presents with: Abnormal pain and swelling, disturbance of bowel motion i.e., constipation or diarrhea, a general constitutional disturbance and fever.	An ultrasonography usually shows matted loops of bowel with free fluid. Peritoneal biopsy rarely done: many of these end up with a laparatomy.
Tuberculous Meningitis	This disease is increasingly frequent with HIV. It is often very difficult to diagnose and requires a very high index of clinical suspicion. This disease presents with: Chronic headache	The diagnosis of tuberculous meningitis rests on: Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: CSF stain positive for mycobacterium.

Miliary TB 	Miliary TB is a result of haematogenous spread. It presents as pyrexia of uncertain cause. Large liver and spleen are common. Choroid tubercles on fundoscopic examination. Miliary lesions on chest X-ray. Night sweats, wasting and other so called constitutional symptoms with very little respiratory symptoms.	Whenever miliary TB is suspected; The eyes should be examined, where feasible, for choroidal tubercles. The chest x-ray shows multiple small millet sized nodular shadows. The diagnosis is rarely confirmed but where facilities are available culture of blood, CSF, liver and blood may be positive for the tubercle bacilli.
Tuberculous Pericarditis 	Tuberculous pericarditis is increasingly becoming common in the HIV era and it may present with a variety of symptoms including: Shortness of breath is the most common symptom. Chest pain. Cough. Leg swelling. Fever. Usually has a high pulse rate (tachycardia). May have a low blood pressure, impalpable apex beat, quiet heart sounds and signs of heart failure like a large liver, ascites and leg edema.	A chest x-ray is always required and usually shows a large globular heart. Where feasible patients suspected to have a pericardial effusion should be referred to a heart specialist for confirmation of the diagnosis using echocardiography. A pericardial tap for diagnostic purpose is rarely required but may be life saving if there are signs of cardiac compression (tamponade). This procedure must be done by experienced health care workers (cardiologists) only.
Tuberculous Meningitis	This disease is increasingly frequent with HIV. It is often very difficult to diagnose and requires a very high index of clinical suspicion. This disease presents with: Chronic headache	The diagnosis of tuberculous meningitis rests on: Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: CSF stain positive for mycobacterium
TB adenitis 	Tuberculous adenitis is one of the common types of extra-pulmonary TB Usually unilateral Most common site is the cervical area Painless swelling –initially discrete then matted Fistula and sinus formation	Node aspirate Node biopsy for both histology and culture

TB encephalitis including Tuberculoma  	The clinical presentation is similar to that of other space occupying brain lesions and includes: • Headaches. • Vomiting. • Convulsions. • Limb weakness. • Cranial nerve palsies.	Brain CT scans are useful in demonstrating lesions. Often it is difficult to confirm the diagnosis of brain TB and most patients are treated on an empiric basis.
	Lupus vulgaris: Persistent and progressive form of cutaneous TB. It occurs as small sharply defined reddish-brown lesions with a gelatinous consistency (called apple-jelly nodules). Untreated, lesions persist for years, leading to disfigurement *Scrofuloderma:* Skin lesions result from direct extension of underlying TB infection of lymph nodes, bone or joints. Often associated with TB of the lungs. Firm, painless lesions that eventually ulcerate with a granular base. May heal even without treatment but this takes years and leaves unsightly scars.	The diagnosis is usually made or confirmed by a skin biopsy. Typical tubercles are caseating epithelioid granulomas that contain acid-fast bacilli. These are detected by tissue staining, culture and polymerase chain reaction (PCR)
NOTE: When patients present with symptoms of TB disease and the health care worker is not able to quickly make a diagnosis or there are signs of severe disease, a rapid referral to the next appropriate level is highly recommended. When health care workers do not know what they are dealing with or do not have the facilities to make a definitive diagnosis or to adequately manage the disease or its complications the patient should immediately be referred to the next appropriate level.		

D. Treatment of TB

The aim of TB treatment

1) Cure patients and therefore prevent suffering and death from TB.
2) Prevent long-term complications or sequelae of TB.
3) Prevent relapse of the disease.
4) Prevent transmission of the infection.
5) Prevent the development of drug resistant TB.

Treatment of tuberculosis benefits both the individual patient and the community as a whole. Any health provider undertaking to treat a patient with tuberculosis is assuming an important public health function that includes not only prescribing an appropriate treatment regimen but also ensuring adherence to the regimen until treatment is completed.

Basic principles of TB treatment

1) Never use single drugs
2) Always use drugs in combinations –using Fixed Dose Combinations (FDCs)
3) Drug dosage is based on weight
4) Drug intake should be directly observed
5) Ensure the entire treatment is taken as recommended

First line anti TB drugs

These are drugs that are prescribed for the treatment of drug sensitive TB. They include:

- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol

These drugs have varying properties.

Table 3.8: Properties of the individual TB drugs

Drug	Mechanism of action	Target bacilli	Media	Compartment it works in
Isoniazid(H)	Bactericidal after 24 hours. High potency: kills >90% bacilli in first few days of treatment.	Rapid and intermediate growing bacilli	Alkaline and acid media.	Intracellular and extracellular
Rifampicin(R)	Bactericidal within 1 hour. High potency. Most effective sterilizing agent.	All populations including dormant bacilli.	Alkaline and acid media.	Intracellular and extracellular
Pyrazinamide (Z)	Bactericidal with a low potency. Achieves its sterilizing action within 2-3 months.	Slow growing bacilli	Acid medium	Intracellular bacilli only (macrophages)
Ethambutol (E)	Bacteriostatic. Low potency. Minimises the emergence of drug resistance.	All bacterial populations.	Alkaline and acid media.	Intracellular and extracellular

Tuberculosis treatment involves the use of multiple drugs taken in combination. These are often combined into Fixed Dose Combinations (FDC) tablets which contain two or more medicines within the same tablet or capsule.

Advantages of using FDCs:

1) Reduced risk of resistance developing to the drugs in the event of missed doses.
2) Reduction of pill burden.
3) Fewer medication errors.
4) Fewer prescription errors.

Disadvantages of FDCs include:

1) Reduced bioavailability of some drugs.
2) Flexibility in obtaining an optimal dose of some agents.

In the first two months of treatment four drugs are used to rapidly reduce bacillary load in the body. This is the **Intensive phase** of anti-TB treatment. After two months, two drugs are used for 4 or 10 months and this is called the **Continuation Phase** of treatment. DOT should be provided using a treatment supporter who is acceptable and accountable to the patient and to the health system.

Table 3.9: Anti TB regimen for use by both adult and children

	Intensive phase	Continuation phase
All forms of TB **except** TB Meningitis and osteo-articular TB	2 RHZE	4 RH
TB Meningitis and osteo-articular TB	2 RHZE	10 RH

Table 3.10: Adult dosage of anti-TB drugs according to body weight

Drug	Recommended dose in mg/kg	Range in mg/kg	Maximum dose
Isoniazid	5	5-10	300mg
Rifampicin	10	10-15	600mg
Pyrazinamide	35	30-40	1.5g
Ethambutol	20	15-25	1.6g

Table 3.11: Pediatric dosage of anti-TB drugs according to body weight

Drug	Recommended dose in mg/kg	Range in mg/kg	Maximum dose
Isoniazid	10	10-15	300mg
Rifampicin	15	10-20	600mg
Pyrazinamide	35	30-40	1.5g
Ethambutol	20	15-25	1.6g

Table 3.12: FDC treatment dosage for adults

FDC Dosages	Formulation	30-39kg	40-54 kg	Over 55 kg
Rifampicin 150 mg + Isoniazid 75 mg + Pyrazinamide 400 mg + Ethambutol 275 mg	4-FDC tablet RHZE	2	3	4
Rifampicin 150 mg + Isoniazid 75mg	2-FDC tablet RH	2	3	4

Table 3.13: FDC treatment dosage for children (5-20kg)

	Intensive phase (2RHZE)			Continuation phase (4RH)	
Weight (kg)	No. of tablets of RHZ in mg (60/30/150)	No. of tablets of RH in mg (60/60)	Ethambutol in mg (100)	No. of tablets of RH in mg (60/60)	No. of tablets of RH in mg (60/60)
5-7	1	1	1	1	1
8-14	2	1	2	2	1
15-20	3	2	3	3	2

Table 3.14: FCD treatment dosage for children (21-30 kg)

	Intensive phase (2 months RHZE)		Continuation phase (4 months RH)	
Weight band (kg)	**No. of adult tablets of RHZE (150/75/400/275mg)**	**No. of paediatric tablets of RH (60/60mg)**	**No. of adult tablets of RH (150/75mg)**	**No. of paediatric tablets of RH (60/60mg)**
21-30	2	2	2	2

Points to note:

1) Monthly monitoring of weight should be done and recorded in the patients TB record card and doses adjusted accordingly.
2) No trial of therapy should be done to minimize emergence of drug resistance.
3) For children above 30kg do not give RH 60/60 but treat as adults
4) All patients taking anti-TBs should also receive daily pyridoxine to reduce the risk of developing peripheral neuropathy. However, lack of pyridoxine should not stop TB therapy.

Table 3.15: Dosages for Pyridoxine

Weight (kg)	Dose of pyridoxine (available in both 25mg and 50mg tablets)
1-13.9 kg	12.5mg
14-25 kg	25mg
>25 kg	50mg

Additional management decisions

a) Hospitalization

The following categories of patients with TB should be treated as in- patients

1) Severe forms of PTB and EPTB (e.g. TB meningitis and pleural effusion) for further investigation and initial management.

2) Severe malnutrition for nutritional rehabilitation.
3) Signs of severe pneumonia (i.e. chest in-drawing).
4) Other co-morbidities e.g. severe anemia
5) Social or logistic reasons to ensure adherence.
6) Severe adverse reactions such as hepatotoxicity.

b) Steroid therapy:

This should be given in the following situations:

1) TB meningitis.
2) PTB with respiratory distress.
3) PTB with airway obstruction by hilar lymph nodes.
4) Severe Miliary TB.
5) Pericardial effusion.

Table 3.16: Dosage of prednisone for adults and children

DOSAGE	Week 1-4	Week5-6	Week7
Adult and Children>30kg	1mg/kg (max 60mg)	0.5mg/kg	0.25mg/kg
Children < 30kg	1-2mg/kg (max 60mg)	0.5-1mg/kg	0.25-0.5 mg/kg

E. Non Tuberculous Mycobacterium (NTM)

Epidemiology

These are free living organisms-found in air, water, soil, from where they cause infection, also zoonotic spread from domestic and wild animals. There is no person to person spread documented. NTM infections are more common in the immune-compromised. There is paucity of data in most of the world, as it is not a notifiable disease. The prevalence is going up, as that of TB is going down.

Local anecdotal data report an incidence of 5-10% of MDRTB sputum culture specimen isolates. There are more than 150 species. The clinically significant mycobacteria other than tuberculosis (NTM) associated with lung disease include: M. avium Complex (MAC), M. kansasii, M. abscesus, M. malmoense, M. szulgai, M. fortuitum, and M. xenopi.

Morphology

All mycobacteria share the characteristic of "acid-fastness," i.e., after staining with carbol-fuchsin or auramine-rhodamine, they do not decolorize with acidified alcohol.
Thus, the common term acid-fast bacilli (AFB) are essentially synonymous with mycobacteria. Microscopy therefore, is less useful in distinguishing between the various types of mycobacteria.

Associated risk factors

- Immune-compromise
- Smoking
- Patients poorly responding to first and second line Anti Tuberculous Therapy
- Previously treated TB patients
- Presence of underlying lung disease

Clinical presentation

- Very similar to PTB-impossible to distinguish clinically, symptoms may include:
- Chronic cough - dry, productive or hemoptysis
- Fever
- Night sweats
- Weight loss-wasting

Suspect atypical organisms in patients with history of previous TB treatment with no poor resolution of symptoms

Investigations

- Sputum smear exam and mantoux test may be positive in both MTB and NTM infection.
- Genexpert will detect MTB **BUT WILL NOT** detect NTM. (*Therefore, in patients with positive AFB sputum smear and a negative GeneXpert result for MTB, consider NTM and obtain a sample for culture*).
- Chest xray and other imaging modalities may also not distinguish between MTB and NTM infection.
- Culture is the gold standard for detection and differentiation of MTB from NTM. Every attempt should be made to obtain a sample for culture when NTM is suspected.

Modalities used to distinguish between the mycobacteria species include:

Culture:

- Appearance on culture media: There are differences in color and sensitivity to light
- Time to produce positive cultures-mycobacteria can be classified into rapidly growing and slow growing mycobacteria

Molecular:

- Line probe assay
- Nucleic acid hybridization probes
- PCR methods

  High performance liquid chromatography

Table 3.17: Management of NTM

Mycobacteria species	Drugs used for treatment	Treatment duration
Mycobacterium Avium complex	• Nodular/bronchiectactic disease: Clarithromycin1gm/Azithromycin 500mg, Rifampin 600 mg and Ethambutol 15-25mg/kg, thrice weekly or daily, +/-amikacin/streptomycin in the first 2-3 months • In HIV co-infection: Substitute rifampicin with rifabutin, daily clarithromycin or azithromycin with ethambutol. Add streptomycin/amikacin if no response • Prophylaxis for all with low CD4 count less than 50: Clarithromycin 1g daily or azithromycin 1g weekly OR a fluoroquinolone if macrolide resistant MAC	Treat until culture negative on therapy for 1 year. Till CD4 above 100.
M. Fortuitum	• Any 2 of the following drugs: Amikacin, fluoroquinolones, sulfonamides, imipenems, linezolid, cefoxitin or clarithromycin • Debridement of cutaneous ,lung or other foci of infection and removal of implants	6-12 months, until cultures are negative
M. Abscessus	• Extremely difficult to eradicate- Multidrug regimens (that include clarithromycin 1g/day and intermittent courses 2 or more drugs of the following drugs: amikacin, imipenem, cefoxitin, tigecycline, fluoroquinolones, doxycycline or linezolid) is recommended may cause symptomatic improvement and disease regression. • Surgical resection of localized disease combined with multidrug clarithromycin-based therapy offers the best chance for cure of this disease.	4-8 weeks of IV drugs then 6-12 months of per oral (P.O) regimen - Treat until sputum is culture negative
M. Kansasii	• Drug susceptible strains- RHZE (use conventional anti-TB doses) • Rifampicin resistant isolates-use any 2 of clarithromycin(1st option) or a fluoroquinolone (if macrolide resistance noted), sulfamethoxazole or streptomycin and ethambutol	- Until sputum cultures negative for more than 6 months
M. szulgai	• Responds to treatment • Combinations of rifampicin, ethambutol and clarithromycin	- Until cultures are negative
M. malmoense	• Not very responsive to treatment • Clarithromycin, rifampicin and ethambutol had better response and less mortality	- At least 2yrs

Summary

Mycobacteria are many different types and most can cause chronic debilitating lung disease.

High index of clinical suspicion is needed to pick atypical mycobacterial infections, particularly in patients with pre-existing lung disease and in those not responding to anti-TBs.

Treatment of atypical mycobacteria is long.

F. TB In Special Populations

I. Tuberculosis in Children

Children comprise up to 15% of all cases of TB among adults. In the context of this guideline, a child refers to a person age 0 to 14 years. This may differ from the definition of children in other contexts.

Diagnosis of TB in children

The diagnosis of TB in children heavily relies on history, physical examination as well as any relevant investigations e.g. TST, CXR and sputum smear microscopy. Even though microbiological diagnosis is not always feasible, all efforts should be made to get a specimen for bacteriological confirmation of TB. A trial treatment with anti-TB drugs is not recommended as a method of diagnosing TB in children.

History

The key elements of history are:

1) History of contact with an adolescent or adult with proven or suspected TB.

Close contact is defined as living in the same household as or in frequent contact with smear positive PTB index case.

If no index case is identified, always ask about anyone in the household/dormitory/ classroom/school transport with chronic cough- if present request assessment of that person for possible TB.

Most children will develop TB within one year of exposure.

2) Symptoms suggestive of TB

The commonest symptoms associated with TB include the following:

- Progressive and non-remitting cough for more than 2 weeks.
- Fever for more than 2 weeks.
- Lethargy /reduced playfulness /less active for more than 2 weeks.
- Weight loss, no weight gain or poor weight gain (failure to thrive).

Physical examination

Examination of the respiratory system
During the physical examination, the following features may be found in the respiratory system:

- Child may have increased respiratory rate.
- Child may have signs of respiratory distress.
- Percussion may be normal. In pleural effusion have a stony dull percussion note.
- Auscultation is frequently normal. May have abnormal sounds (e.g. wheezing, crackles, bronchial breathing).

In some cases, there may be atypical clinical presentations of PTB. In this case the child will present with features of:

a) Acute severe pneumonia

- Presents with fast breathing and chest in-drawing
- Occurs especially in infants and HIV-infected children

Suspect PTB if response to antibiotic therapy is poor. If child is HIV infected also suspect other HIV-related lung disease e.g. PCP.

b) Wheeze
Asymmetrical and persistent wheeze can be caused by airway compression due to enlarged tuberculous hilar lymph nodes. Suspect PTB when wheeze is asymmetrical, persistent and non-responsive to bronchodilator therapy.

PTB can also present acutely as bronchopneumonia in children with tachypnea, respiratory distress and crackles.

A normal respiratory clinical finding does not rule out PTB.

Examination of the other systems

TB can affect any part of the body apart from the hair, nails and teeth. Apart from the general physical features suggestive of TB, a child may also present with features that are specific to the affected system e.g. in TB meningitis a child may have features of raised intracranial pressure or neurological deficit.

This further increases the need to have a thorough physical examination.

Simplified Clinical TB Diagnosis

Having taken history, done a physical examination, Mantoux and chest x-ray where available, the health worker may at this point make a clinical diagnosis of PTB in the child as summarized below and make decisions on treatment.

Simplified clinical diagnosis of TB

Presence of 2 or more of the following symptoms
Cough >2weeks
Weight loss or poor weight gain
Persistent fever and/or night sweats>2weeks
Fatigue, reduced playfulness, less active
PLUS
Presence of 2 or more of the following:
Positive contact history
Respiratory signs
CXR suggestive of PTB (where available)
Positive Mantoux test (where available)
Then PTB is likely, and treatment is justified

Investigations

After history and physical examination, if investigations are available in the facility or nearby, attempt should be made to investigate every child suspected to have TB. Tests that are used for diagnosis include:

1. GeneXpert

This is the preferred test for diagnosis of TB among children where available and is done for Sputum, gastric aspirate, CSF and bronchial secretion specimens.
Specimens from children who cannot expectorate can be obtained through a gastric aspirate or sputum induction (Annex).

2. Sputum microscopy

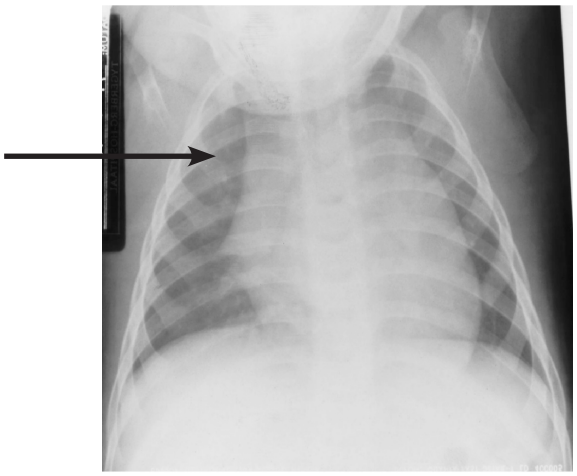
Where GeneXpert is not available, the sputum specimen can be evaluated using sputum microscopy.

3. Chest Xray

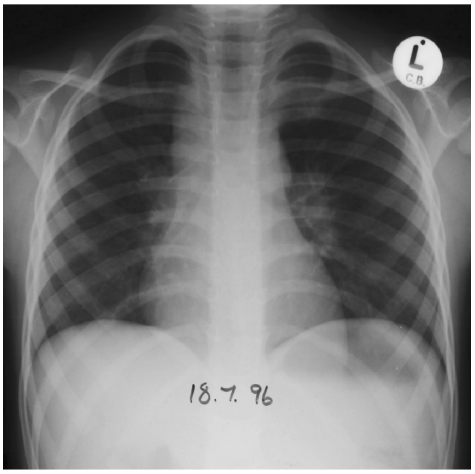
TB may present with diffuse disease in younger children and an adult-like cavitary picture in older children. Radiological features suggestive of PTB will include:

- Persistent lung opacification especially if focal
- Enlarged hilar or subcarinal lymph nodes. In children below 6 years of age, mediastinal widening may be due to the thymus gland
- Diffuse micronodular infiltrates (miliary pattern)
- Pleural effusions
- Upper lobe opacification with or without cavities especially in adolescents.

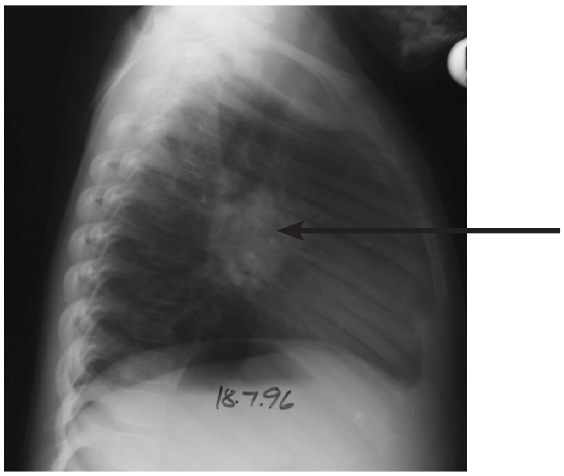
Pictures suggestive of Pulmonary TB



Common cause for a widened mediastinum in a young child is a large thymus which causes the sail sign on the chest radiograph (see arrow).



Suspected hilar and paratracheal lymph gland enlargement. The diagnosis can be made with more certainty when a lateral chest radiograph is examined as well



Massive hilar lymph gland enlargement visible on the lateral chest radiograph. The arrow indicates the hilar lymph glands.

I. Mantoux

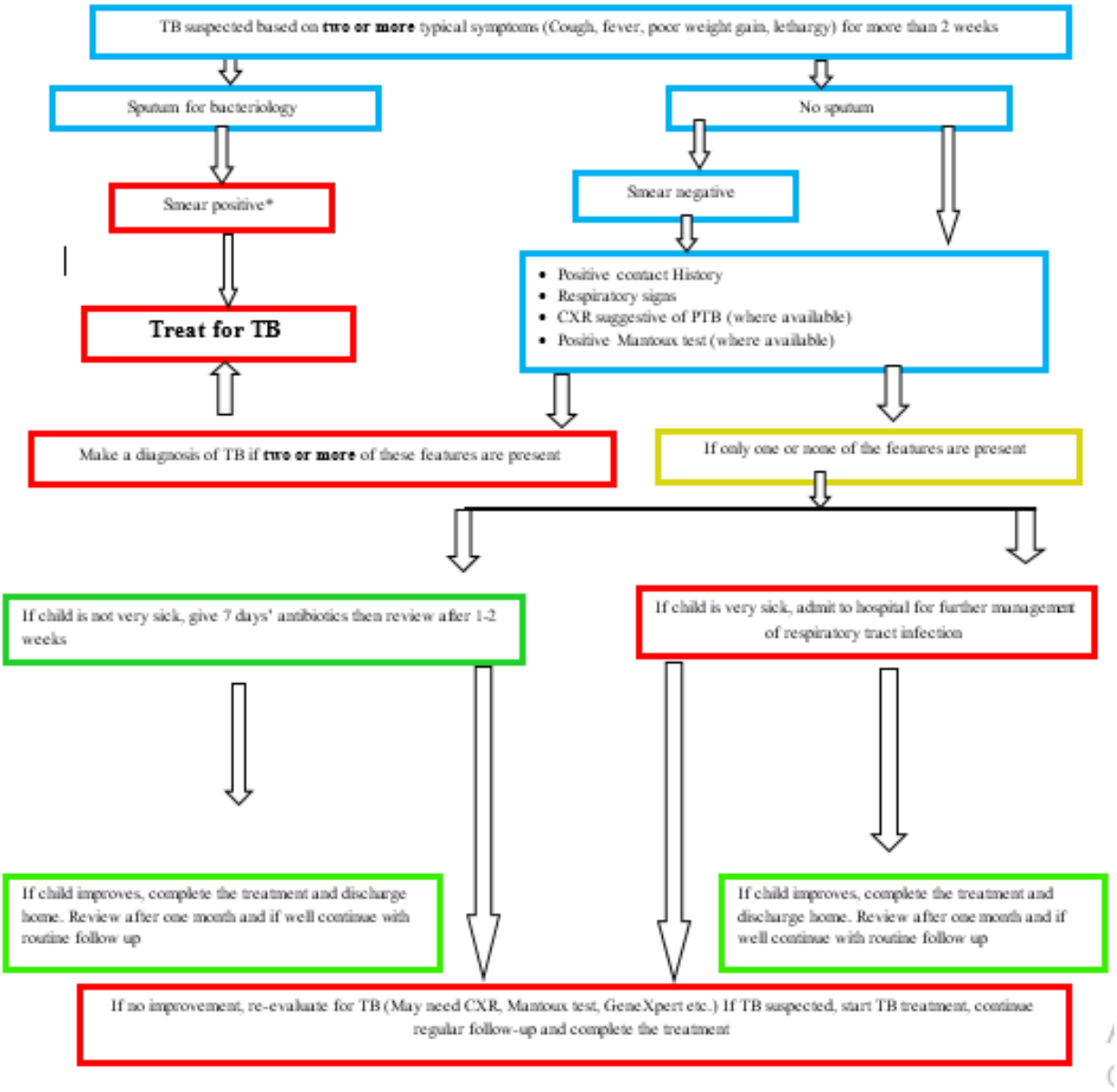
A positive Mantoux test is evidence that one is infected with M. Tuberculosis, but doesn't necessarily indicate disease. Correct technique of administering, reading and interpretation of Mantoux text is very important (Annex).

Mantoux is positive if induration is:

- ≥10mm in a well-nourished, HIV negative child
- ≥5mm in a malnourished, or HIV infected child

A negative Mantoux does not rule out TB (especially in the HIV positive or malnourished child).

Figure 3.6: Algorithm for TB Diagnosis in Children



Note:

*Smear Positive result can be obtained from microscopy for GeneXpert, microscopy or TB culture. GeneXpert is preferred as a first test in children.

1. All children with TB should be tested for HIV and all children with HIV should be screened for TB
2. Mantoux test should be regarded as positive if:
    - >5mm diameter of induration in high risk children (includes HIV-infected, immune-suppressed and severely malnourished children)
    - >10 mm diameter of induration in other children (whether they have received vaccination or not)
3. Please note that a Mantoux may be negative despite the child having TB especially in severe disseminated TB, malnutrition and HIV disease
4. A child in close contact with smear positive household member should be considered TB infected and TST may not be necessary.

Table 3.18: Differential diagnosis for Child with chronic cough/respiratory symptoms	
Possible diagnosis	**Clinical presentation**
Asthma	Recurrent wheeze/cough – responds to bronchodilators. Usually associated with other allergies such as eczema, rhinitis
Upper airway conditions **Allergic rhinitis** **Adenoid hypertrophy**	Recurrent / persistent runny nose and /or nasal blockage and snoring. Seasonal pattern triggers.
Foreign Body Inhalation	Usually sudden onset in previously well child May have history of choking Persistent cough One sided respiratory signs–inspiratory stridor, wheeze
Gastro-esophageal reflux disease	Recurrent cough/wheeze Onset in early infancy +/- hoarse voice
Bronchiectasis	Severe persistent cough, much sputum (often infected green or yellow in colour). Finger clubbing. CXR shows reticular or honey-comb pattern.
Congenital Heart Disease	Easy fatiguability, breathlessness, Onset early infancy
Acquired heart disease	Older children, palpitations, easy fatiguability, dyspnoea on exertion. +/- oedema
Congenital respiratory disorders	Onset early infancy Commonly premature baby Noisy breathing during inspiration not responding to bronchodilators

Extra-Pulmonary Tuberculosis (EPTB) in Children

Extra pulmonary TB is common in children and presentation varies with age. Symptoms are usually persistent and progressive with the most common form being TB lymphadenitis. Clinical assessment in all cases of EPTB should consider:

- Time lapse from exposure to disease presentation can be quite variable– shorter for young children with disseminated disease, longer for other forms that present in school-aged children.
- Common symptoms present in most cases of EPTB include fever, weight loss/ poor weight gain, and lethargy/reduced play lasting >2weeks. Symptoms and signs specific to the site of EPTB as shown in the Table 3.19.
- Investigations for TB as appropriate according to site of infection.

In addition to fever, weight loss, lethargy lasting more than 2 weeks and history of contact, suspect extra-pulmonary TB if the child also has clinical features suggested in table 2. This table lists typical clinical features for various forms of EPTB and suggested investigations for each category.

Table 3.19: Diagnosis of Extra Pulmonary TB in children

Site of EPTB	Typical clinical presentation	Investigation	Comment
TB lymphadenitis	- Asymmetrical, painless, non-tender lymph node enlargement for more than one month+/- discharging sinus - Most commonly in neck area	Fine needle aspiration when possible Mantoux	Treat
Pleural TB	Dullness on percussion Reduced breath sounds +/-chest pain	CXR Pleural tap[1]	- If pleural fluid is straw colored, treat for TB. - If pleural tap reveals pus consider Empyema and refer
TB meningitis	Headache, irritability/ abnormal behavior, lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanel, cranial nerve palsies	- Lumbar puncture to obtain CSF[2] - Infants-cranial ultrasound - Older child do CT scan brain - Mantoux test	Hospitalize for TB treatment
Miliary TB	Non-specific, lethargic, fever, wasted	- CXR - Mantoux test	Treat and refer[3] where appropriate
Abdominal TB	Painless abdominal Swelling with ascites	- Ascitictap[1] - Abdominal ultra-sound[4] - Mantoux test	Refer[3] where appropriate
Spinal TB	- Painless deformity of spine - May have lower limb weakness/paralysis	- Lateral X-ray spine - Mantoux test	Refer where appropriate[3]
Pericardial TB	- Cardiac failure - Distant heart sounds - Apex beat difficult to palpate	- CXR - Echocardiogram - Mantoux test	Refer[3] where appropriate

[1]Typical findings: straw colored fluid, exudates with high protein, white blood cells especially lymphocytes
[2]Require 2 - 5ml of CSF.
[3]Referral may be necessary for investigation procedure and laboratory support as well as clinical care. If referral is difficult or not readily available, start anti-TB treatment. The above table highlights the more common forms of EPTB; however TB may infect other organs.
[4]Abdominal ultra-sound illustrates abdominal lymphadenopathy and shows complex ascites+/- septation.

TB bone and joint (excluding spine)	-Painless, non-tender swelling end of long bones with limitation of movement -Painless, non-tender unilateral effusion of usually knee or hip	-X-ray of affected bone and/ or joint - Joint tap - Mantoux test	Refer[3] where appropriate

Treatment of Tuberculosis in Children

Some of the important points to note about TB treatment in children are:

- Children usually have paucibacillary disease, as cavitating disease is relatively rare (about 6% or less) in children under 13 years of age and the majority of the organisms in adult-type disease are found in cavities.
- Children develop extra-pulmonary TB (EPTB) more often than do adults.
- Severe and disseminated TB (e.g., TB meningitis and miliary TB) occur especially in young children (less than 3 years old).
- Treatment outcomes in children are generally good even in the HIV infected provided treatment is started promptly. However, response to treatment in this category may be slow.
- Children generally tolerate the anti-TB drugs better than adults.
- Dosages are calculated according to weight (not age)
- Weight is important for monitoring treatment response
- TB drugs are very well tolerated in children
- Streptomycin is no longer recommended as first-line therapy in children

Standard Operating Procedures for Treatment

- Classify the case of child TB before starting treatment into pulmonary or extrapulmonary TB,
- Record the TB diagnostic category, treatment regimen and date anti-TB treatment was started on road-to-health book as well as on TB treatment card and facility TB register.
- A caregiver should be identified as the DOT supporter for all ages including older children. Educate the DOT supporter on anti-TB regimen and adherence.
- Take the child's weight at each visit and record.
- Calculate drug dosages at every visit according to the child's current weight (note that children gain weight while receiving anti-TB treatment).
- Once treatment is started it must be completed; **"trial of TB treatment" should never be used as a diagnostic tool**

Recommended Treatment Regimen

The table below shows the currently recommended TB treatment regimen in children.

Table 3.20: WHO Recommended TB Treatment Regimen For Children

TB disease category	Recommended regimen	
	Intensive phase	Continuation phase
All forms of TB except TB meningitis, bone and joint TB (osteoarticular TB)	2˙ RHZE	4 RH
TB meningitis *Osteoarticular TB*	2 RHZE	10 RH
Drug resistant TB	Refer to a DRTB specialist	

Use of Ethambutol in children

Ethambutol is now recommended as fourth drug in intensive phase of first-line regimens. The risk of toxicity is negligible for children of any age when Ethambutol is used at recommended dosages of **20(15-25) mg/kg/day.** Thus Ethambutol can be safely used at recommended dosages in all ages but dosage should not exceed 25mg/kg/day.

Risk of toxicity is dose-related and related to duration of therapy. The main potential side-effect is optic neuritis that can lead to blindness. However, the data on risk of toxicity in children has been extensively reviewed and there is now a lot of clinical experience of its use in young children.

Ethambutol can be safely used in all children of all ages at recommended dosages of 20mg/kg

Young age influences drug metabolism: a particular dose of a drug in mg/kg when given to a young child (under 5 years) may not reach the same level in the blood as when given to an older child or adult. Higher mg/kg dosages are therefore required in young children to achieve levels that are considered to produce effective bactericidal activity.

Table 3.21: Dosages for Pediatric TB treatment using dispersible FDC tablets of RHZ, RH and single Ethambutol tablets (Child between 5 and 20 kg)

	Intensive phase (2 months RHZE)			Continuation phase (4 months RH)	
Weight band (kg)	No. of tablets of RHZ (60/30/150mg)	No. of tablets of RH (60/60mg)	Ethambutol (100mg)	No. of tablets of RH (60/30mg)	No. of tablets of RH (60/60mg)
5 - 7.9	1	1	1	1	1
8- 14.9	2	1	2	2	1
15 -20.9	3	2	3	3	2

Table 3.22: Dosages for Pediatric TB treatment using dispersible FDC tablets of RHZ, RH and single Ethambutol tablets (Child between 21 and 30kg)

	Intensive phase (2 months RHZE)		Continuation phase (4 months RH)	
Weight band (kg)	**No. of tablets of RHZE (150/75/400/275mg)**	**No. of tablets of RH (60/60mg)**	**No. of tablets of RH (150/75mg)**	**No. of tablets of RH (60/60mg)**
21-30.9	2	2	2	2

Note: For children above 30kg, do not give RH 60/60 but treat as adults
All children must be on pyridoxine 12.5mg/day

Table 3.23: Dosages for Pediatric TB treatment using NEW FDC tablets of RHZ, RH and single Ethambutol tablets

	Numbers of tablets		
	Intensive Phase		Continuation Phase
Weight bands	**RHZ (75/50/150mg)**	**E(100mg)**	**RH(75/50mg)**
4-7kg	1	1	1
8-11kg	2	2	2
12-15kg	3	3	3
16-24 kg	4	4	4
25 kg+	Use adult dosages and preparations		

Additional Management Decisions

a) Hospitalization

The following categories of children with TB should be treated as in-patients:

- Severe forms of PTB and EPTB (e.g. Spinal TB) for further investigation and initial management.
- TB meningitis.
- Severe malnutrition for nutritional rehabilitation.
- Signs of severe pneumonia(i.e. chest in-drawing).
- Other co-morbidities e.g. severe anaemia.
- Social or logistic reasons to ensure adherence.
- Severe adverse reactions such as hepatotoxicity.

b) Steroid therapy

This should be given in the following situations:

- TB meningitis
- PTB with respiratory distress
- PTB with airway obstruction by hilar lymph nodes

- Severe Milliary TB
- Pericardial effusion

Give prednisone at **2mg/kg** once daily for 4 weeks, and then taper down over 2 weeks **(1mg/kg for 7 days, then 0.5mg/kg for 7 days)**

c) Referral of children with TB should be considered if:

- Child has severe disease.
- Diagnosis is uncertain.
- Necessity for HIV-related care to commence ART.
- Failure to respond to treatment despite good adherence.

d) Pyridoxine

Give pyridoxine to all children on TB treatment. This is to reduce the risk of these children developing peripheral neuropathy due to Isoniazid. The dosage is as shown below:

Isoniazid Preventive Therapy (IPT) in children

Provide Isoniazid preventive therapy (IPT) for the following high risk children in whom signs or symptoms of TB disease have been ruled out:

- All children aged under 5 years who have been exposed to a case of infectious TB irrespective of their HIV status
- All HIV infected children above one year.
- HIV infected children under one year of age who have been exposed to a case of infectious TB.

Follow up of a child on IPT is monthly. If TB disease develops, stop IPT and treat for TB.
All children on IPT should receive pyridoxine at **12.5mg daily**.

Note: **INH preventive therapy should NOT be given to children exposed to an adult with proven MDR/XDR TB. The children should instead be followed up for signs of active TB disease and managed appropriately**.

Table 3.24: Dose of Isoniazid (INH) for Isoniazid Preventive Therapy (IPT) in children

Weight (kg)	Daily Dose in mg	Number of 100 mg tablets
<5	50	½
5.1 – 9.9	100	1
10-13.9	150	1½
14-19.9	200	2
20-24.9	250	2½
>25	300	3*

*For children more than 25 kg, one can use 1 adult tablet of INH (300mg) once daily.

All children on IPT should also receive pyridoxine at 12.5mg/day.

Children on IPT should receive monthly follow up. During the follow up visit:

- Continuously reinforce message of adherence.
- Screen for TB disease i.e. persistent cough, fever, lethargy, poor weight gain
- Monitor INH adverse effects.
- Maintain a contact register.

Follow-up of a child on anti-TB Therapy

This is a critical part of effective TB treatment.

Patients visit the health facility weekly during intensive phase and every two weeks during continuation phase. During the visit, the child should be assessed for:

- Adherence
- Drug toxicity
- Weight gain
- Symptom assessment

Sputum should be taken for AFBs at months 2, 5 and 6 for those who were smear positive at the beginning of treatment.
The following should be done at each visit:

- Weigh the child at each visit. Document the weight and adjust dosage if necessary.
- Address adherence issues.
- Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better.
- Note risk factors for poor adherence such as long distance to health facility, lack of/ transport costs, orphan (especially if mother has died) or primary care-giver unwell and adolescents.
- Education and adherence support especially TB/HIV. Explain that anti-TB drugs in children are well tolerated and safe.

CXR is not required in follow-up if the child is responding well to anti-TB treatment

Poor response to treatment

Most children with TB will start to show signs of improvement within 4 – 8 weeks of anti-TB treatment. Weight gain is a sensitive indicator of good response to treatment. Children not responding to TB treatment after one month should be reassessed for causes of the poor response and possible drug resistance. **TB treatment should however not be stopped.**

Potential causes of poor response to treatment include:

- Poor adherence; this is the commonest cause. If uncertain, a child can have health care worker DOT at the health facility.
- HIV infection.
- Wrong diagnosis.
- Other concurrent chronic lung diseases.
- Under dosage of drugs Resistant form of TB Complications e.g. neurological complications, bronchiectasis e.t.c.

Consider treatment failure if child is receiving anti-TB treatment and:

- There is no symptom resolution or symptoms are getting worse. In this case, always confirm adherence is good. If uncertain, a child can have health care worker DOT at the health facility.
- There is continued weight loss.
- If smear positive at baseline and remains smear positive up to 5 months.

Refer children with suspected treatment failure for further assessment.

Ways to improve adherence

- Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better.
- Note risk factors for poor adherence such as distance/transport; orphan (especially if mother has died) or primary care-giver unwell; adolescents.
- Education and adherence support especially TB/HIV.
- Explain that anti-TB drugs in children are well tolerated and safe.

Treatment Interruptions

To be managed as per the adult regulations.

Adverse drug reactions of anti TB drugs in children

The most important side-effect is hepatitis which may present with nausea and vomiting. Presence of abdominal pain, jaundice and tender enlarged liver suggest severe hepatotoxicity. Stop the anti-TB drugs immediately and refer to hospital.

INH may cause symptomatic pyridoxine deficiency, particularly in severely malnourished children and HIV infected children on highly active antiretroviral therapy (HAART). It manifests as tingling, numbness and weakness. A child may also present with reduced playfulness. Supplemental pyridoxine is recommended.

Other side effects occur in a similar way to the adults and are managed in the same way.

Follow up during treatment

Each child should be clinically assessed every 2 weeks during the intensive phase, and every month during the continuation phase until treatment completion. The assessment should include:

- Symptom assessment
- Assessment of adherence by reviewing the treatment card
- Inquiry about any adverse events
- Weight measurement
- Drug dosage adjustment to account for any weight gain

All drug dosages should be adjusted to account for any weight gain

A follow-up sputum smear for microscopy at 2 months should be obtained for any child who was smear-positive at diagnosis. **Follow-up chest radiographs are not routinely required in children, who are improving on treatment as radiological changes usually lag behind clinical response.**

A child who is not responding to TB treatment should be assessed for adherence and drug resistance.

TB and HIV Co-Infection in Children

Diagnosis of TB in HIV

Approach to diagnosis of TB in HIV infected children is similar as for HIV uninfected children. History of contact with TB is extremely important in pointing to possibility of TB disease in a younger, HIV infected child.

The clinical presentation of TB is similar between those in early stages of HIV disease and those without HIV. However, those with advanced HIV disease may not have the typical TB clinical features, and chronic respiratory symptoms may be due to other causes. They may also present with extra pulmonary TB. HIV test is indicated in all children with suspected TB. Tuberculin Skin Test (Mantoux test) may be negative. Together with TB symptoms, positive Mantoux test is indicative of TB disease. Positive Mantoux test without symptoms or features suggestive of TB should not be used to diagnose TB (see algorithm for TB diagnosis in children, chapter 3).

Differential Diagnosis in HIV infected Child with Chronic Respiratory Symptoms

The diagnosis of PTB can be particularly challenging in a HIV-infected child because of clinical and radiological overlap with other HIV-related lung disease. Other possible causes of chronic lung disease in HIV infected children are shown in the Table 3.25:

Table 3.25: Differential diagnosis of chronic respiratory symptoms in HIV infected children

Differential Diagnosis	Clinical features
Recurrent pneumonia	Recurrent episodes of cough, fever and fast breathing that usually respond to antibiotics
Lymphoid Interstitial Pneumonitis	Slow onset cough associated with generalized symmetrical lymphadenopathy, finger clubbing, parotid enlargement. Nutritional status variable, mild hypoxia, CXR: diffuse reticulonodular pattern and bilateral perihilar adenopathy
Pneumocystis Jirovecii Pneumonia	Common cause of acute severe pneumonia, severe hypoxia especially in infants. Unusual after 1 year. CXR: diffuseinterstitialinfiltration,hyperinflation

Tuberculosis	Persistent respiratory symptoms not responding to antibiotics. Often poor nutritional status; positive TB contact especially in younger children CXR: focalabnormalitiesandperihilaradenopathy
Bronchiectasis	Cough, productive of purulent sputum, halitosis, finger clubbing, seen in older children. CXR: honeycombing usually of lower lobes Complicates recurrent bacterial pneumonia, LIP or TB
Mixed infection	Common problem: LIP, bacterial pneumonia, Consider TB when there is poor response to first-line empiric management
Kaposi's sarcoma	Uncommon Characteristiclesions onskinorpalate

Treatment of TB in HIV in Children

The principles of treatment of tuberculosis in HIV-infected children are similar to those in HIV-negative children, and the same regimens should be used as those used in HIV negative children. Response to TB treatment may be slow in PLWHA. All children with TB/HIV should receive co-trimoxazole prophylaxis as well as antiretroviral therapy. Nutritional support is often needed for children with TB/HIV. The management of children with TB/HIV should be integrated so that all family members are counseled and tested for HIV, screened for TB and managed appropriately. ARVs should be initiated within 2-8 weeks of starting anti-TB therapy.

Cotrimoxazole Prophylaxis

Commence cotrimoxazole prophylaxis. Commence antiretroviral therapy within 2– 8 weeks of starting anti-TB therapy. Conduct family-based care/screening for HIV.

Immune re-constitution inflammatory syndrome (IRIS)

This is a paradoxical deterioration after initial improvement following treatment initiation. It is seen during the initial weeks of TB treatment with initial worsening of symptoms due to immune re-constitution. IRIS is commonly seen in the severely immuno-compromised TB/HIV co- infected child after initiating ARV treatment.

Management: Continue anti-TB therapy: give non-steroidal anti-inflammatory drugs until severe symptoms subside.

IPT among children with HIV infection

All HIV infected children above one year and all HIV infected children under one year of age who have been exposed to a case of infectious TB should be given IPT once active TB disease has been ruled out as per the guidelines.

Prevention of TB in HIV

All HIV-infected children have to be screened for TB using the ICF/IPT tool (Annex). All HIV infected children exposed to sputum smear positive TB case should be evaluated for TB and treated if diagnosed with TB disease. Those without TB disease should be offered Isoniazid preventive therapy at **10mg/kg/day** for 6 months.

All TB infected children should be offered counseling and testing for HIV infection. Known HIV infected children should minimize their exposure to other patients with chronic cough (e.g. separate waiting area, or fast track their consultation from the waiting area).

The specific needs of each family should be determined and a plan of action developed to ensure that the family receives comprehensive care using all available services.

Deliberate efforts be made to expand the prevention of mother to child transmission. This is because minimizing HIV infection in children will reduce their risks of developing TB. Thus all pregnant mothers should be tested for HIV. Those found to be HIV positive should be initiated on IPT if TB disease is ruled out. TB screening should be continued after the baby is born for both mother and baby.

BCG vaccine is to be given to all new born babies except those with symptoms of severe HIV infection. It is also not given to children started on IPT before its administration. In these children complete the IPT course and wait 2 weeks after IPT completion to give BCG.
Always examine the placenta for tubercles as their presence may implicate vertical TB transmission.

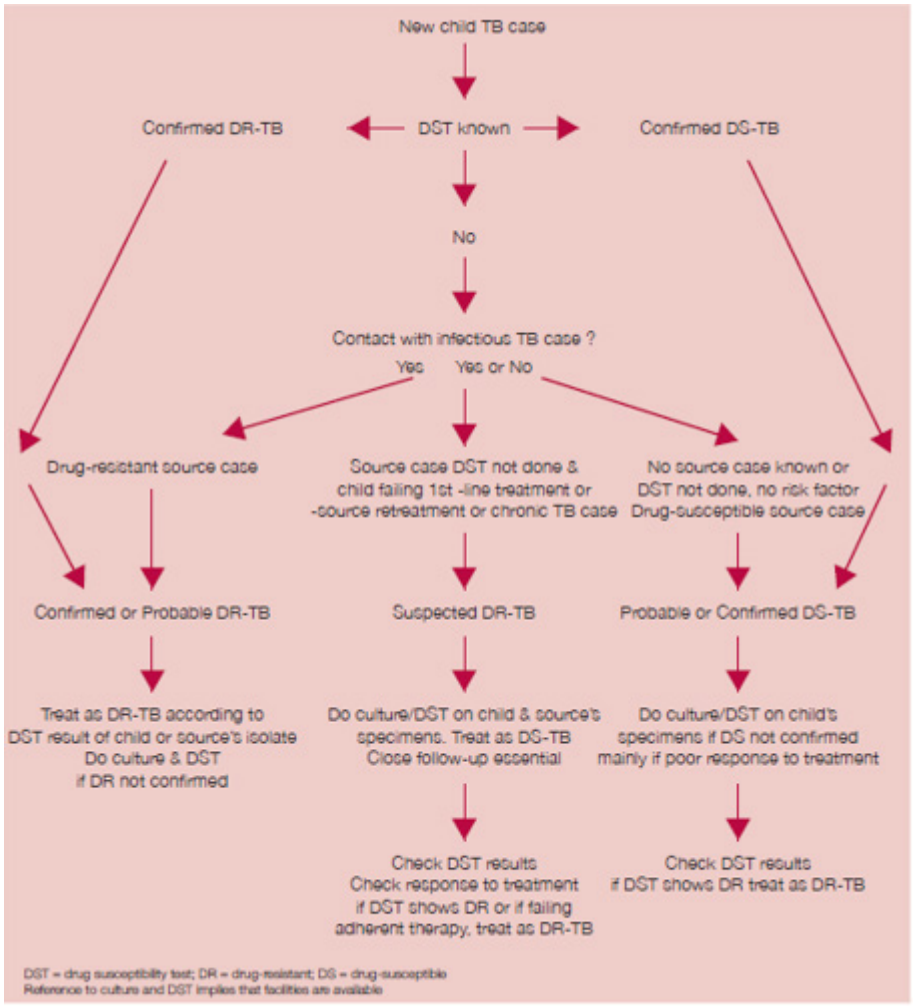
Drug Resistant TB (DR TB) in Children

Drug-resistant TB should be suspected when:

- There is contact with known DR-TB.
- There is contact with suspected DR-TB, i.e. source case is a treatment failure or a retreatment case or recently died from TB.
- Child with TB is not responding to first-line therapy despite adherence.
- A child previously treated for TB presents with recurrence of disease.

When DR-TB is suspected, every effort should be made to confirm the diagnosis by obtaining specimens for culture and drug susceptibility testing (DST). The recommended diagnostic algorithm for diagnosis should be followed.

Figure 3.7: Diagnostic algorithm for the diagnosis of DR-TB in children



Management of child contacts of drug-resistant TB

Current WHO guidelines do not recommend preventive therapy for contacts of DR-TB patients.

Close contacts of DR-TB patients who develop TB disease usually have drug-resistant disease.

All children with a DR TB contact should be screened for TB disease and if not found to have TB disease they should be followed up every 2-3 months for the first 6 months, then 6-monthly for at least 2 years. If TB disease develops, treatment with an appropriate DR-TB regimen based on the DST pattern of the presumed source case should be initiated.
Care providers should note that younger children are more at risk of progressing to TB disease.

Treatment of DR TB in children

The treatment of monoresistant TB, polyresistant TB, MDR-TB and XDR-TB in children is guided by the same principles and uses the same second-line drugs as the treatment in adults. Children with MDR-TB generally have poorer treatment outcomes and higher mortality than those with drug-sensitive TB. For MDR TB and XDR TB, treat the child according to the

DST results from the likely source case, unless M. *tuberculosis* culture and DST results are available from the child. It is safe to use fluoroquinolones for the treatment of DR TB in children. Follow up of children on DR TB treatment is as that of adults.

TB Prevention in Children

Screening for child contacts of known TB cases

Young children living in close contact with an index case of smear positive pulmonary TB are at a high risk of TB infection and disease. The risk of infection is greatest if the contact is close and prolonged. The risk of developing disease after infection is much greater for malnourished children, children under 5 years and HIV infected children than it is for HIV un-infected children and those over 5 years. If the disease develops it usually does so within 2 years of infection, but in infants the time lag can be as short as a few weeks.

Isoniazid preventive therapy (IPT) for young children with infection who have not yet developed disease will greatly reduce the likelihood of developing TB during childhood.

Contact screening refers to the screening or evaluation for TB infection or disease of all children who are close contacts of smear positive PTB index case. Contact tracing should be done for all infectious cases of PTB.

The main purpose of child contact screening is to:

1. Identify symptomatic children (i.e. children of any age with undiagnosed TB disease) and treat them for TB.
2. Provide Isoniazid preventive therapy (IPT) for the high risk children who have no signs or symptoms of TB disease.

Generally a simple clinical assessment is sufficient to decide whether the contact is well or symptomatic. This can be done through evaluation of signs and symptoms guided by a set of questions in a screening tool (Annex). Contacts and source cases should be counseled and tested for HIV. Contacts of DR TB should be managed according to guidelines.

BCG Vaccination in Children

BCG is a live attenuated vaccine derived from M. Bovis. It offers protection against the more severe types of TB such as Milliary TB and TB meningitis, which are common in young children. All children should be given the BCG vaccine as soon as possible after birth EXCEPT those with suspected TB infection at birth and with severe HIV infection. In children with suspected TB infection or disease, the BCG vaccination should then be deferred till 2 weeks after completion of IPT/TB treatment.

A child who has not had routine neonatal BCG immunization and has symptoms of HIV disease/ congenital immunodeficiency syndrome should also not be given BCG because of the risk of disseminated BCG disease.

A small number of children (1–2%) may develop complications following BCG vaccination. These commonly include:

- Local abscesses at the injection site
- Secondary bacterial infections

- Suppurative adenitis in the regional axillary lymph node
- Local keloid formation
- Disseminated BCG disease. If axillary node enlargement is on the same side as BCG in a HIV- positive infant, consider BCG disease and refer.

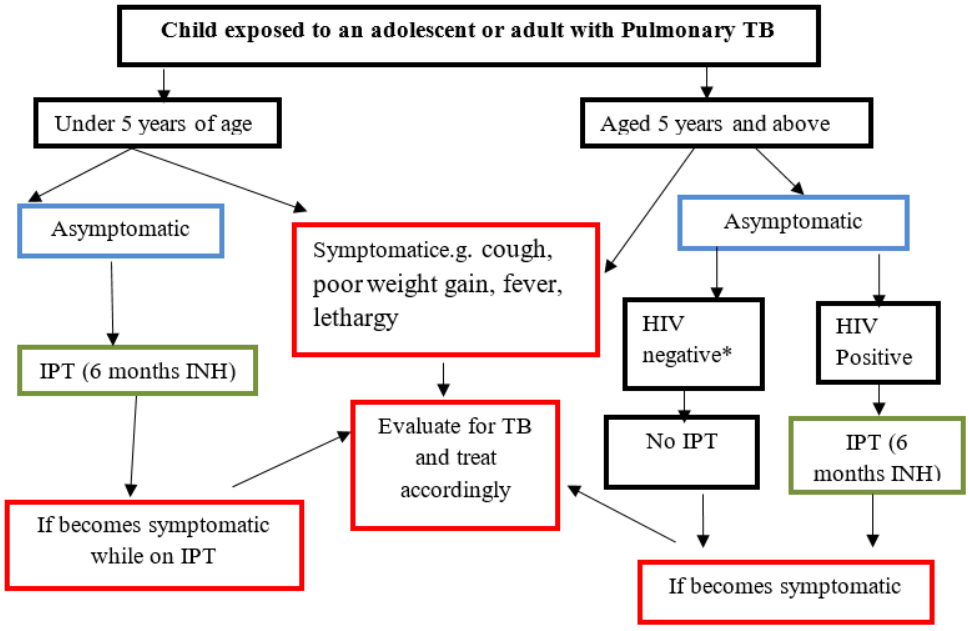
Most reactions will resolve spontaneously over a few months and do not require specific treatment. Children who develop disseminated BCG disease should be investigated for immune-deficiencies and treated for TB using a 4-drug first-line regimen: 2RHZE then 4RH (The BCG bacillus has poor susceptibility to Pyrazinamide).

Child Nutrition and TB

Malnutrition is an important public health issue particularly for children under five years of age who have a significantly higher risk of mortality and morbidity than well-nourished children. In Kenya, the infant and the under-five mortality rates are 77 and 115 per 1000 live births respectively. The national figure for acute malnutrition of children under five years old is estimated at 6%.

One of the key indicators for clinical monitoring in children being treated for TB is improvement in nutrition status. There are several ways to monitor the nutrition status of undergoing TB treatment. All children should have a baseline weight and height. The weight is then assessed at every visit and appropriate drug adjustments made in case of weight gain.

Figure 3.8: Management of a child who has been exposed to an adolescent or adult with Pulmonary TB



*Asymptomatic HIV negative child older than 5 years and not on IPT should be followed up every 3 months for at least 1 year.

Any child who is symptomatic should be evaluated for TB disease and treated accordingly.

Parent should be advised to bring the child to the hospital any time the child develops symptoms.

For children 0-59 months of age their age, weight and height/ length are taken and Z–Scores documented as per the reference charts. For children 5-17 years their age, weight and height are used to assess the BMI for age (Annex).

Table 3.26: Anthropometric criteria to identify severe, moderate and at risk categories of acute malnutrition for children and adolescents*

Indicator	Severe Acute Malnutrition (SAM)	Moderate Acute Malnutrition (MAM)	At Risk of Acute Malnutrition
Infants less than 6 months			
W/L	W/L < - 3 Z-Score	Static weight or losing weight at home	Static weight or losing weight at home. Z-Score
Oedema	Oedema Present	Oedema Absent	Oedema Absent
Other signs	Too weak to suckle or feed	Poor feeding	Poor feeding
Children 6 months to 10 years			
W / H Z-Scores	< -3 Z-Score	Between -3 to < -2 ZScore	Between -2 to <-1 Z-Score
Oedema	Oedema Present	Oedema Absent	Oedema Absent
Adolescent (10 years to 18 years)			
Oedema	Oedema Present	Oedema Absent	Oedema Absent

**Anthropometric criteria based on WHO Child Growth Standards (2006)*

II. TB/HIV Co-Infection

The human immunodeficiency virus (HIV) pandemic presents a significant challenge to global tuberculosis (TB) control. TB is a leading preventable cause of death among people living with HIV. Despite this close epidemiological links between HIV and TB, the public health responses have largely been separate, and have so far had little success in interrupting the sequence of events by which HIV infection fuels the TB epidemic. Better coordination of HIV and TB program activities is needed to mitigate the dual epidemic of TB/HIV in populations at risk of or affected by both diseases. TB and HIV programmes have to collaborate and carry out joint activities aimed at combating the two diseases.

Relationship of TB and HIV/AIDS

In the decades leading up-to 1980, TB was on a decline throughout the world, and there was reason to believe that if control efforts were maintained, and where necessary strengthened, TB would be driven steadily towards elimination. This scenario changed with the advent of the HIV/AIDS pandemic, to the extent that even well performing control programmes have not been sufficient in containing TB where HIV infection rates are high.

TB is the leading cause of death among PLHIV and in countries with advanced epidemics, particularly those in sub-Saharan Africa, the majority of TB patients are also infected with HIV. In some countries the proportion of TB patients dually infected with HIV is as high as 70%. HIV is also the most common known risk factor for endogenous reactivation of latent TB infection to active disease or exogenous re-infection. HIV positive individuals have a 50% lifetime risk of developing tuberculosis with an annual risk of 5-15%. This risk has been shown to increase with declining CD4+ counts.

These statistics show that there is a strong epidemiological justification for TB and HIV programmes to develop joint activities to tackle the dual menace. TB and HIV programmes need to exploit synergies in supporting health service providers to deliver joint interventions. It is known that the burden of TB is so closely linked to the HIV epidemic that prevention of HIV must become a priority for TB programmes. TB care and prevention should also be a major concern for HIV/AIDS programmes. There has been progress in the implementation of basic essentials for control of HIV-related TB in most countries and what generally used to be perceived as low priority in HIV prevalence countries is now changing.

Ways in which the two diseases interact with each other are listed below

Interaction of HIV with TB
1. Increased lifetime risk of TB from 5-10% to 50%
2. Increased rate of progression of new TB infections to disease
3. Increased risk of recurrence of previously treated TB
4. Increased risk of death from TB
5. Increased risk of adverse reactions to anti-TB drugs
6. Increased stigma to the two diseases
Interaction of TB with HIV
1. Rapid progression of HIV disease
2. TB is the leading cause of HIV-related morbidity
3. TB is a leading cause of mortality among PLHIV (one-third of all AIDS related deaths are due to TB)
4. Increasing TB cases among PLHIV enhances the risk of TB transmission in the community regardless of their HIV status

Table 3.27: Collaborative TB/HIV activities implemented in various settings

Objective/ Activity	Implementer
A. **Establish the mechanism for collaboration** 1. TB/HIV coordinating bodies 2. HIV surveillance among TB patient 3. TB/HIV planning 4. TB/HIV monitoring and evaluation	**TB and HIV Programmes**

B. **To decrease the burden of TB in PLHIV- Three Is** 1. Intensified TB case finding 2. Isoniazid preventive therapy 3. TB infection control in health care and other settings	**HIV programme**
C. **To decrease the burden of HIV in TB patients** 1. HIV testing and counselling 2. HIV prevention 3. Cotrimoxazole preventive therapy 4. HIV/AIDS care and support 5. Antiretroviral therapy to TB/HIV co-infected patients	**TB programme**

Coordination of TB/HIV collaborative activities

For effective implementation of TB/HIV collaborative activities, there must be good coordination. It is recommended that every county and sub county should establish TB/HIV coordinating committees.

Coordinating County and Sub county TB/HIV activities
The coordinating officers should be able to encourage collaborative activities and have the capacity to document and monitor such activities. The coordinating committee should identify existing resources that can be used for coordination. Practical steps to planning the implementation of TB/HIV collaborative activities at the sub-county

Sub county situation analysis

This includes analysis of the TB/HIV services:

- Collection of TB/HIV baseline statistics
- The identification of risk groups for TB and HIV infection
- A survey of existing sub county TB and HIV/AIDS service providers
- A survey of existing stakeholders in the area

This will be the responsibility of the sub-county Health Management Team (sCHMT) in consultation with the SCTLC and SCASCO.

Sources of information include:

- HMIS.
- Sub county TB register.
- Laboratory, ward and OPD registers.
- Surveillance results if they exist.
- Morbidity and mortality records.

Situational analysis should include description of groups within the sub county considered to be at special risk of TB and/or HIV infection e. g. groups of people known to be infected with HIV and PLHIV support groups, patients with STI's, prisoners, the military, CSW, IDU's and migrant groups like seasonal laborers.

A list of service providers should be included with an assessment of their;

- Target population/catchment area
- Number of clients/patients using service
- Gender and ages of patients/clients
- HIV status of patients/clients
- Drugs available for HIV care at different clinical service providers

Trends of service use over time should also be collected and the list should include:

- Who is doing what and where in TB and HIV care provision.
- Identification of gaps in the package of prevention and care for HIV and TB within the sub county
- Identification of underserved populations

Establishing a TB and HIV/AIDS coordinating committee

The County Health Management Team, sCHMT, Facility HMT, should establish a coordinating committee with all the relevant TB and HIV/AIDS care and support stakeholders invited to participate. Terms of reference and reporting structure for the group should be defined. This committee should be meeting regularly to enable effective networking and collaborative activities.

A chairperson and secretary should be elected during the formation of the steering committee. The elected chair should preferably come from non-government stakeholders within the sub county while the secretary should be from the Ministry of Health.

For purposes of proper implementation, coordination and supervision of TB/HIV collaborative activities, the committees should initially be meeting monthly and then quarterly to review implementation of activities and task officers. Minutes of the previous meeting should be shared before the next meeting is called.

Where feasible, health institutions should set up health facilities committees that will offer an opportunity for these institutions to address implementation constraints and to plan for reducing transmission of both TB and HIV in the institutions. The steering committees will ultimately strengthen the delivery of health care to all patients.

Establishing a referral system

In many areas, a number of TB and HIV/AIDS service providers already exist but often work in isolation. The result is that a network of care and support does not exist in the sub county despite the presence of comprehensive TB/HIV care and support providers. One of the first priorities for the coordinating committee is to establish links between the service providers at all levels in order to create a patient-centered referral system. The committee should seek to strengthen existing sub county referral systems so that patients with other illnesses can

also benefit from the improved system. Referrals within the health facility, to and from the community should also be strengthened and made easy for the patients.

Supporting the staff

There is need to constantly have support supervision to identify strengths and weakness and motivate staff. Sub county TB/HIV committees should invest time and resources in training and motivating TB/HIV service providers as new activities are planned and implemented within the sub county. Other activities to support the staff include:

- Regular meetings to maintain and update the skills of the service providers
- Confidential staff support meetings where staff can share their own emotional responses to the occupational stress
- Regular supervision with supportive and constructive feedback to health care providers
- Exchange visits with care providers in other sub-counties and Health facilities
- Strategies to reduce the risk of TB and HIV in health staff

Monitoring and evaluation

Make recording and reporting routine. There should be quarterly collection of data from partners on service use. This will allow changes in the sub county TB/HIV service performance to be monitored. Indicators for new activities should also be monitored and reported quarterly. Six monthly and yearly evaluations should be undertaken including quarterly meetings where lessons learned can be exchanged.

Documenting the process

The coordinator of the sub county collaborative activities should be responsible for documenting the process of planning and implementing collaborative TB/HIV activities including the resources required.

Assessing the cost of the work plan

Some finances may be allocated to the sub county/county from the national TB/HIV budget. However, other sources of funding should be explored to keep activities going:

- NGO's, CBOs
- Faith-based organizations
- Charities
- Local companies
- Private business

Provider Initiated Testing and Counseling (PITC)

This is HIV testing initiated by a health worker as part of the diagnostic work up for patients who present with symptoms or signs that could be attributable to HIV disease. This will offer an entry point for all TB patients to quality and comprehensive treatment and care. TB patients tested for HIV who turn out to be HIV positive should immediately be initiated on Cotrimoxazole Preventive Therapy (CPT). Immediate ARVs should be initiated within 2 to 8 weeks from the time of TB/HIV diagnosis based on the ART guidelines.

Sites for HIV testing of TB patients will depend on several factors within the institution including but not limited to workload, space for testing and human resources available. However, the common areas where the HIV testing can be done include:

- At the chest clinic
- At the laboratory
- A side room next to the TB clinic/ward
- At the VCT site

If HIV testing is done in other areas apart from the chest clinic, measures such as escorted referrals should be put in place to ensure that the TB patients are not lost during referral and that they do not queue for long while waiting to be attended. Issues of confidentiality should always be addressed and a member of staff should be tasked to take results to the clinician. PITC provides an entry point for provision of HIV prevention methods including those in the PwP package like disclosure of HIV status, partner testing, condom promotion, STI care, adherence counseling, risk reduction, etc. All HIV positive patients on the other hand should be screened for TB using the TB ICF symptom screening tool. Investigate those with signs and symptoms of TB to rule out active disease.

Management of TB and HIV Co-Infected Patients

Cotrimoxazole preventive therapy (CPT) reduces mortality among TB patients with HIV irrespective of CD4 count. Therefore be provided to all TB/HIV co infected individuals (unless contraindicated). Should be monitored for side effects including rash and gastrointestinal disturbance. Cotrimoxazole should be withdrawn whenever moderate to severe reactions occur.

Table 3.28: Dose of Contrimoxazole for CPT

Weight in kg	Cotrimoxazole syrup (mg per ml)	480 mg (Single Strength) tablet	960 mg (Double strength) tablet
1.0 - 4.9	2.5mls	¼ tab	-
5.0 - 8.9	5mls	½ tab	¼ tab
9.0 - 16.9	10mls	1 tab	½ tab
17.0 - 30.9	15mls	2 tab	1 tab
>30.9 (adults and adolescents)	-	2 tab	1 tab

Dapsone is recommended in patients allergic to Cotrimoxazole (CTX) and is used only in patients with WHO stage 4 disease and /or those with a CD4 <200 cells /mm^3.

Dapsone should be discontinued when:

- the CD4 has been greater than 200 cells /mm3 for adults and children >5 years for at least 6 months
- the CD4% has been greater than the age specific threshold for severe immunodeficiency in the young children for at least 6 months

Dose for Dapsone

Dapsone is available as 25mg and 100 mg tablets.

- Children: 2mg / kg once daily (maximum dose 100mg)
- Adults: 100mg once daily

Provision of Anti-Retroviral Therapy

All TB /HIV co-infected patients should be started on ART irrespective of CD4 count. Recent evidence shows that early initiation of ART reduces mortality and improves TB outcomes.

Table 3.29: ART in Adolescents and Adults with TB/HIV Co-Infection

TB patient newly diagnosed with HIV (ART-naive) • Start TB treatment immediately as per the national TB guidelines • If ART-naive, start ART after TB treatment is tolerated, within 2-8 weeks		
Scenario	**ART regimen**	**Comments**
Newly diagnosed HIV in a TB patient(ART naive)	Preferred: TDF + 3TC + EFV Alternative: AZT + 3TC + EFV	Continue same ART regimen after completing TB treatment. ART is not considered to be failing within 6 months of initiation
Patient develops TB while on ART Carry out a viral load(VL) test if patient has been on ART for a period of more than 6 months and does not have a recent undetectable viral load; change the first line regimen to an appropriate 2nd line regimen if treatment failure is confirmed		
If on NVP-based first line ART Regimen	Change NVP to EFV	Assess for treatment failure • Continue additional adherence counseling and support
If on LPV/r or ATV/r-based Regimen	Continue current regimen and use **Rifabutin (150mggiven once daily)** instead of rifampicin* for TB treatment*Rifampicin use with LPV/r or ATV/r should be avoided due to drug interactions. In circumstances where Rifabutin is not available, alternative options include •Superboost LPV/r with ritonavir to make LPV:Ritonavir ration to 1:1 •Double the dose of LPV/r Note: These two scenarios increases intolerability to LPV/r hence preference for Rifabutin	Assess for treatment failure •Continue additional adherence counseling and support

Table 3.30: ART in Children with TB/HIV Co-Infection

Children newly diagnosed with TB and HIV (ART naïve)

- Start TB treatment immediately as per the national TB guidelines
- Start appropriate ART after TB treatment is tolerated, preferably within 2-8 weeks

Age	Preferred regimen	Alternative regimen	Comments
0-3 years	ABC + 3TC + LPV/r + RTV (add extra dose of RTV to make the LPV/RTV ratio 1:1 (super boosted LPV)	AZT + 3TC+LPV/r ABC + 3TC + EFV* AZT + 3TC + EFV* ABC + 3TC + AZT**	***Note: US FDA has approved use of EFV in children 3 months old and above and weighing more than 3.5 kg. Currently in Kenya, use of EFV in children aged < 3 years and weighing < 10 kg is recommended ONLY in TB/ HIV co-infection management without prior exposure to NVP for PMTCT** **ABC + 3TC + AZT (triple nucleoside) is an inferior regimen and should only be used if other regimens are not tolerated. After completion of TB treatment, change the triple nucleoside based ART regimen to ABC + 3TC + LPV/r
≥3-10 years	ABC + 3TC + EFV	AZT + 3TC + EFV	
>10-14 years	(<35 kgs) ABC + 3TC+ EFV (>35 kgs) TDF + 3TC + EFV	AZT + 3TC + EFV	

Table 3.31: Child develops TB while on ART

Child develops TB while on ART

Assess for treatment failure if patient has been on ART for a period of more than 6 months change the first line regimen to an appropriate 2nd line regimen if treatment failure is confirmed

Age	Current regimen	Recommended ART substitution while on TB treatment	Comment
0-10 years	If EFV-based ART	Continue EFV-based ART	Conduct viral load to rule out treatment failure and manage as per the national Guidelines
	If NVP-based ART	Change NVP to EFV	
	If LPV/r-based ART	Super boost LPV/r (LPV : Ritonavir= 1:1)	Switch back to normal dose of LPV/r after completion of TB treatment Conduct viral load to rule out treatment failure and manage as per the national Guidelines

> 10 yrs		**Alternative:** Triple nucleoside ofABC+3TC+AZT	Please note that triple nucleoside is an inferior regimen and should only be used in children not able to tolerate super-boosted LPV/r. Triple nucleoside should not be used in children who have failed 1st line ART; in such cases clinician should consult/refer to a specialist for management. Switch back to LPV/r-based regimen after completion of TB treatment
	EFV-based ART	Continue EFV-based ART	Conduct viral load to rule out treatment failure and manage as per the national guidelines
	NVP-based ART	Change NVP to EFV	
	If LPV/r-based ART	If < 35 kg weight: Super boost LPV/r (LPV:Ritonavir = 1:1) with Rifampicin-based TB treatment	Switch back to normal dose of LPV/r after completion of TB treatment. Conduct viral load to rule out treatment failure and manage as per the national guidelines.
		If weight is > 35 kg: Continue current regimen and use **Rifabutin (150mg once daily)** instead of Rifampicin	Conduct viral load to rule out treatment failure and manage as per the national guidelines.
Note: Rifabutin dosing for TB treatment in TB/HIV patients on PI based ART has been reviewed. Rifabutin should be administered as **ONCE DAILY** dosing of 150 mg instead of 150 mg three times a week alongside other anti-TB drugs.			

Table 3.32: Efavirenz Dosing in Children

Weight (kg)	EFV dose (mg)*	No. of tablets (200mg double scored tablet)
3.5 to 4.9	100	½ tab
5 to 7.4	150	¾ tab
7.5 to 13.9	200	1 tab
14 to 19.9	300	1 ½ tabs
20 to 24.9	300	1 ½ tabs
25 to 34.9	400	2 tabs
35 and above	600	3 tabs (or 1 tablet of 600mg)

Table 3. 33: Ritonavir dosing for super-boosting LPV/r in children taking Rifampicin

Weight Range (kg)	Lopinavir/ Ritonavir (LPV/r)		
	TWICE Daily	TWICE Daily	TWICE Daily
	80mg Lopinavir/ 20mg Ritonavir per ml solution	200mg Lopinavir /50mg Ritonavir tablets	Ritonavir liquid (80mg/ml, in 90 ml bottle) Ritonavir dose is adjusted to nearest mark for the ease of measurement
3 - 5.9	1.5 ml	-	1 ml
6 - 9.9	1.5 ml	-	1 ml
10 - 13.9	2 ml	-	1.5 ml
14 - 19.9	2.5ml	1 tab	2ml or 2 of 100mg capsules
20 - 24.9	3 ml	1 tab	2.5 ml or 2 of 100mg capsules
25 - 34.9	4 ml	2 tab in am & 1 tab in pm	4 ml in am & 2 ml in pm or 2 of 100mg capsules in morning and 3 of 100mg capsules in evening

Intensive Case Finding and Isoniazid Preventive Therapy

- Symptom-based TB screening using ICF tool MUST be done for all PLHIV at every visit to rule out active TB. Each patient file should have an ICF tool
- Investigations for TB should be performed in accordance with existing national guidelines
- Chest radiography is not required as part of routine screening; however patients deemed to be TB suspects, should have a chest X-ray where sputum is unavailable

Infection control measures should be given priority to reduce TB transmission in all settings that provide patient care

Indications for Isoniazid Preventive Therapy

- HIV-infected children less than 12 months of age who have had recent close contact (past 12 months) with sputum positive TB disease with no evidence of active TB.
- All PLHIV above 12 months of age (including pregnant and breastfeeding women) who screen negative for TB disease.
- All children under 5 years of age irrespective of HIV status who have had recent close contact (past 12 months) with sputum positive TB disease with no evidence of TB disease.
- Prisoners who screen negative for TB disease irrespective of HIV status.
- TB patients with HIV co-infection who have just completed their course of TB treatment.

- Health care workers
- TB infection with no evidence of TB disease--in these 2 categories, are we saying that we shoulld give IPT or one day we shall give?

Note:

- **Past history of TB and current pregnancy are not contraindications for starting Isoniazid preventive therapy.**
- IPT has not been shown to increase the risk of developing Isoniazid-resistant TB.
- Currently, once the patient has completed the 6 month course of IPT, repeating the course of IPT is not recommended.

Duration and Dose of INH for IPT

IPT should be given at a dose of 10 mg/kg/day (maximum 300 mg) for duration of 6 months

Table 3.34: Duration and Dose of INH for IPT

Weight (kgs)	Dose in mg	Number of 100mg INH tablets	Number of 300mg INH tablets
<5	50	½ tablet	-
5.1-9.9	100	1 tablet	-
10-13.9	150	1 ½ tablet	½ tablet
14-19.9	200	2 tablets	-
20-24.9	250	2 ½ tablets	-
>24.9	300	3 tablets	1 tablet
Adults	300	-	1 tablet

Dosing of Pyridoxine for All Patients taking Isoniazid

All patients taking INH (whether for IPT or TB treatment) should also receive daily pyridoxine to reduce the risk of developing peripheral neuropathy. However, pyridoxine should not be a barrier in initiation of IPT.

Dose of pyridoxine

Table 3.35: Dose of Pyridoxine

Weight (kg)	Number of tablets of pyridoxine (50mg)
5-7	(1/4) quarter tablet daily
8-14	(1/2) half tablet daily
≥ 15	(1) one full tablet daily

Follow up of patients on IPT

All patients on IPT should be reviewed monthly and adherence messages reinforced at every visit. At every visit ensure:

- Patient is screened for active TB using the intensive case finding (ICF) tool
- Patient's ICF cards and IPT register records are updated and outcome documented on completion of therapy
- Patient is monitored for INH adverse events (co administer with pyridoxine to minimize adverse events)

The facility should maintain a TB contact register to help in identifying patients eligible for IPT.

Contraindications to IPT

- Active hepatitis (acute or chronic)
- Regular and heavy alcohol consumption
- Symptoms of peripheral neuropathy
- IPT should be discontinued in symptomatic patients with ALT/AST more than three times the upper normal limits

Use of Xpert MTB/Rif (GeneXpert) in Diagnosis of TB for PLHIV

GeneXpert is a molecular diagnostic test for TB disease that can detect *Mycobacterium tuberculosis* DNA and Rifampicin resistance from sputum specimen in less than 2 hours.

This technology is more sensitive than sputum microscopy in detecting TB. In addition, its ability to detect smear negative TB provides added advantage in people living with HIV.

GeneXpert is increasingly available in Kenya and is now recommended by the Ministry of Health for TB diagnosis in all HIV- infected persons suspected to have TB.

Note: Refer to the algorithm on "Use of GeneXpert for Diagnosis of Drug Resistance and surveillance of TB

III. TB and Diabetes

Diabetes triples the risk of developing tuberculosis (TB). Consequently, rates of TB are higher in people with diabetes than in the general population, and diabetes is a common co-morbidity in people with TB. Diabetes can worsen the clinical course of TB, and TB can worsen glycemic control in people with diabetes. Individuals with both conditions thus require careful clinical management. Strategies are needed to ensure that optimal care is provided to patients with both diseases: TB must be diagnosed early in people with diabetes, and diabetes must be diagnosed early in people with TB. TB and DM preventive messages should be given in both care settings as patient education and CMEs to the facility staff. IPT is **NOT** recommended as a method of preventing TB in DM patients (studies have shown that there may not be any additional benefit to this and it may worsen peripheral neuropathy associated with DM).

In 2013, the International Diabetes Federation (IDF) estimated there to be 387 million people worldwide living with diabetes, of whom 46.3% were undiagnosed. The prevalence of diabetes was 8.3% worldwide with 77% occurring in low and middle income countries with 4.9 million deaths in 2014. There were 775,200 cases of diabetes in Kenya in 2014 and the estimated prevalence among the adult population (20-79 years) in Kenya is 3.6%.

Improved collaborative activities would improve care and prevention of diabetes. Under-diagnosis of the disease is common, and could be improved by screening people with TB for diabetes. Management of diabetes must be optimized in general, and in particular during TB disease, as during all types of infections. Improved management of diabetes could build on the successes of the DOTS strategy, emphasizing support to patients and supervision of their treatment; standardized protocols, a reliable supply of quality-assured medicines, regular monitoring and evaluation, and management and administrative procedures; as well as political commitment.

The objective of collaborative activities to improve care and prevention of diabetes are:

1. Set up means of coordinating diabetes and TB activities.

This could be included in the TB/HIV County, sub county and facility level task forces.

2. Detect and manage TB in patients with diabetes

This includes;

a) TB screening that should be done for diabetic patients at every visit using the National TB ICF/IPT symptom-screening tool.

b) This should be recorded in the individual patients TB ICF/IPT symptom-screening card and aggregated in the National presumptive TB register.

c) Sputum smear microscopy should be used to investigate the patient for TB or genexpert if it is available. Other appropriate investigations like radiography and culture should conducted as recommended for any other TB patient. Healthcare workers in the diabetes clinic should provide DOTs TB treatment as per the National guidelines.

d) Upon completion of TB treatment, patients with diabetes should be referred back to a specialist diabetes clinic for continued diabetes chronic care and management.

3. Detect and manage diabetes in patients with TB

It is essential to note the following;

a) All TB patients co-morbid with DM are treated with the same standard regimen.

b) All attempts should be made to ensure glycemic control is optimum during TB treatment. This may include regular random and fasting sugar monitoring at every clinical visit, and as often as possible based on glycemic control.

c) Sputum monitoring of co-morbid TB/DM patients will be conducted as is the case for TB patients without DM.

4. Ensure TB infection control in health-care settings where diabetes is managed

In diabetes clinics, where the risk of TB is higher than in the general population, the risk of transmitting TB is increased, and the consequence of transmission is more severe for a person with diabetes. As is commonly practiced within the TB settings, Infection Prevention and Control interventions, including administrative, environmental and respiratory measures should be implemented.

IV. TB in Pregnancy and Lactation

TB in pregnancy

Worldwide, the burden of tuberculosis (TB) disease in pregnant women is substantial. In 2011, it was estimated that more than 200,000 cases of active tuberculosis occurred among pregcore nant women globally; the greatest burdens were in Africa and Southeast Asia. The pathogenesis of tuberculosis infection and disease in pregnant women is similar to that in non-pregnant women. TB in pregnancy however, can present insidiously, since symptoms of malaise and fatigue may be attributed to pregnancy rather than disease. In addition, during pregnancy it can be difficult to recognize weight loss.

Since pregnancy has not been shown to increase the risk of TB, the epidemiology of TB in pregnancy is a reflection of the general incidence of disease in the general population. Pregnant women with active TB disease should be treated as soon as the diagnosis of TB has been made with the standard 6 month regimen 2RHZE/4RH. These anti TBs are not dangerous in pregnancy and are compatible with breast feeding. Adherence to anti-TBs will cure tuberculosis, and prevent spreading tuberculosis to the unborn child as well as the household. Identification and treatment of maternal TB is the best way of preventing TB in the newborn. There is no significant increase in malformations for infants born to infected mothers and there is also no indication for therapeutic abortion.

Peri-natal Tuberculosis and Lactation

Breast feeding should be continued during anti-TB therapy as the excretion of these drugs through breast milk is minimal and does not affect neonates and infants. These trace amounts of anti-TB in breast milk are however not enough to treat or prevent TB in the neonate, and children born to mothers with TB must therefore be evaluated for TB as well.

TB prophylaxis among neonates and infants

Neonates born to mothers with active TB who screen negative for TB should be offered Isoniazid Preventive Therapy (IPT) prophylaxis. BCG is then offered 2 weeks after completion of the 6 month course of IPT. Refer to IPT and pyridoxine dosages. Though extremely rare, intrauterine transmission of TB may occur. Once a baby is born to a mother with active TB disease, or an infant has close contact with active TB disease, the following steps should be undertaken:

- Evaluate for clinical features of perinatal tuberculosis
  These may be present at birth or delayed until eight weeks of age. They are non-specific and may include:-
  - Respiratory distress
  - Fever
  - Hepato-splenomegaly
  - Irritability, poor feeding and lethargy
  - Lymphadenopathy
  - Failure to thrive
  - Jaundice

- Where TB is diagnosed
  If neonatal TB is suspected, conduct gastric aspirates for sputum gene Xpert, Chest x-ray, and lumbar puncture where indicated. On confirmation of TB, initiate anti TBs, using the standard 6 month regimen (2RHZE/4RH) alongside pyridoxine. Breastfeeding should be continued until the child is 6 months. BCG for neonates on anti-TBs should be withheld until 2 weeks after completion of the anti-TBs.

V. TB in Prison

TB in prisons is a major public health problem in many settings, particularly in countries with a high incidence of TB. In Kenya, the TB notification rate in prisons is 10 times higher than in the general population. The situation is worsened by the emergence and spread of drug-resistant TB, particularly multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

The following should be noted about TB in prisons;

a) All presumptive TB cases (i.e screening positive) within the prison population should be investigated using GeneXpert as the preferred confirmatory test
b) Treatment should be administered under the direct observation of health care staff
c) IPC measures should be observed to reduce transmission
d) All TB patients should be tested for HIV, and those testing positive initiated on CPT and ART immediately
e) Upon transfer or release from the prison, prisoners on treatment should be referred using the referral forms to a facility for continuity of care

VI. TB and Alcohol Abuse

All TB patients must be asked about history of alcohol use to identify people with those with harmful drinking habits and or alcohol dependence as this could impact negatively on TB treatment outcomes. This should be recorded in the TB patient record card.
The following should be done:

1. Identify the risks and discuss the consequences of alcohol abuse.
2. Provide medical advice on the benefits and consequences of alcohol abuse.
3. Solicit patient commitment to reducing / stopping alcohol use.
4. Identify goals e.g. reduced drinking or abstinence.
5. Give advice and encouragement to stop drinking.
6. Provide educational materials on alcohol cessation and abstinence.
7. Screen for other co-morbidities particularly liver and kidney dysfunction.

VII. TB and Tobacco Use

All TB patients should be evaluated for smoking and tobacco use. Identify smokers among new TB patients and enquire on duration of smoking, number of cigarettes smoked per day including previous history of smoking. This should be recorded in the TB patient treatment card.

1. Discourage smoking by offering counseling and education on the dangers of smoking to themselves and others in their vicinity.
2. Explain that cessation will improve the patient's chances of getting cured; preventing TB related death and not spreading TB infection at home.
3. Positive benefits on smoking cessation should be highlighted such as saving money, gaining health; protecting family members from the effects of second hand smoke and improved physical performance.
4. Address any barriers they may have to quitting smoking.
5. A smoking cessation plan with set timelines should be drawn out together with the patient who is willing to quit smoking.
6. Assess the progress of the smoking cessation plan at every appointment and record this in the TB patient record card.

G. Drug Resistant TB

I. Programmatic Management of Drug Resistant Tuberculosis in Kenya

Introduction

Globally, it is estimated that 480 000 cases developed MDR TB in 2014. This is approximately 5% of all TB cases. Annually, about 150 000 die due to this form of tuberculosis and that about 9% of these cases developed XDR-TB. In 2012, WHO estimated 450,000 MDR TB cases of whom 170,000 died.

Kenya is one of the 22 high burden TB countries that collectively contribute about 80% of the world's TB burden. In 2014 there were 99,179 TB cases in the country of whom 9, 879 (9.6%) were previously treated. WHO estimates in 2012 that 2.5% of the new smear positive cases and 10% of previously treated patients have MDR TB leading to a total of 2,780 cases of MDR TB. Kenya achieved a treatment success rate of 83% in MDR TB for the 2012 cohort.

Causes of Drug Resistant TB

The main cause of drug resistant TB is due to Mycobacteria's genetic machinery to mutate at a certain rate and still keep on growing, enabling them to survive otherwise effective anti-TB drugs.

There are two principal pathways leading to the development of active drug-resistant TB:

(i) Acquired (secondary) drug resistance

(ii) Primary drug resistance.

Primary or initial drug Acquired drug resistance is the result of inadequate, incomplete or poor treatment quality that allows the selection of mutant resistant strains as a result of:-

Table 3.36: Causes of drug resistant TB

Health care provider factors	Drugs	Patients factors
Absence of guidelines, Non compliance to guidelines, inadequate training, poor or no treatment monitoring , poorly organized or funded TB control programmes.	Inadequate supply, poor quality, poor storage conditions, wrong dose or combination, poor regulations of medicines, unavailability of certain medicines	Poor adhearance or poor DOT, lack of information, lack of transportation, adverse effects, social barriers, malabsorption, substance dependency disorder , HIV, diabetes mellitus, psychiatric conditions.

II. Classification of Drug Resistance

Classification based on drug resistance

Cases are classified in categories based on drug susceptibility testing (DST) of clinical isolates confirmed to be *M. tuberculosis*:

Table 3.37: Classification of drug resistant TB based on drug susceptibility testing (DST) of clinical isolates confirmed to be M. tuberculosis

Monoresistance	Resistance to one first-line anti-TB drug only
Polydrug resistance (PDR TB)	Resistance to more than one first-line anti-TB drug (other than both Isoniazid and Rifampicin)
Rifampicin resistance (RR TB)	Resistance to Rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to Rifampicin, whether monoresistance, multidrug resistance, Polydrug resistance or extensive drug resistance
Multidrug resistance (MDR TB)	Resistance to at least both Isoniazid and Rifampicin
Pre–XDR	Resistance to Isoniazid and Rifampin and either a fluoroquinolone or a second-line injectable agent but not both
Extensive drug resistance (XDR TB)	Resistance to any Fluoroquinolone and to at least one of three second-line injectable drugs (Capreomycin, Kanamycin and Amikacin), in addition to multidrug resistance.
Presumptive drug resistant TB cases	This is a diagnosis given to patients who have a high risk of getting MDR TB than the general population. They include: smear positive previously treated patients such as relapse, return after default (RAD) and failure; new smear positive pulmonary TB patients whose sputum remains smear positive at month 2; symptomatic close contacts of known MDR-TB patient, refugees, prisoners, health care workers with symptoms of TB, DR TB contacts.

III. Registration of DR TB patients

Before enrolling patients on second line drugs, one needs to establish whether s/he has previously received any anti-tuberculosis treatment, whether for drug sensitive TB or drug resistant TB, and if so, when and the treatment outcome during that illness was. The following categories are used for registration:

Table 3.38: Registration of Drug Resistant TB Patients

New (N)	Patients who have never received anti-tuberculosis treatment, or who have received anti-tuberculosis treatment for less than one month. (Note: patients who had DST at the start or within one month of a WHO regimen and are then switched to a Category IV regimen because of resistance are placed in this group, even if they received more than one month of Category I treatment).
Relapse (R)	Patients previously treated for tuberculosis that has been declared cured or treatment completed, and then diagnosed with MDR-TB.
Return after loss to follow up	Patients who return to treatment with confirmed MDR-TB after interruption of treatment for two months or more
After failure of First Line Treatment (FFT)	Patients who return after having failed the first treatment i.e. smear positive at earliest, month 5
After failure of Retreatment FRT)	Patients who return after having failed the re-treatment.
Transfer in (TI)	Patients who have been transferred from another register for treatment of drug-resistant TB to second line treatment. Their outcomes should be reported to the transferring unit so that it can report their outcomes in the cohort in which they originally started MDR-TB treatment.

IV. Treatment Outcomes for Drug-Resistant Patients

Table 3.39: Definitions of Treatment Outcomes for Drug-Resistant Patients

Cured	DRTB patient who completes treatment with three or more consecutive negative cultures taken at least 30 days apart after the intensive phase.
Treatment completed	DRTB patient who has completed Treatment as recommended Without evidence of failure BUT no record that three or more Consecutive cultures taken at least 30 days apart are negative after the intensive phase.
Death	A patient who dies from any cause while on DR-TB treatment.

Loss to Follow Ups	A patient who interrupts DR-TB treatment for two or more consecutive Months.
Treatment failure:	Treatment terminated or need for permanent regimen change of at Least two anti-TB drugs because of: • Lack of conversion by end of the intensive phase; or • Bacteriological reversion in the continuation phase after conversion to negative • Evidence of additional acquired resistance to fluoroquinolones or Second-line injectable drugs; or • Adverse drug reactions
Transfer out	A patient who has been transferred to a reporting unit in another County and for whom the treatment outcome is unknown.
Not evaluated	A patient for whom no treatment outcome assigned. (This includes cases "transferred out" to another treatment unit and whose treatment outcome is unknown).
Treatment success	The sum of Cured and Treatment completed.

For Treatment failed, lack of conversion by the end of the intensive phase implies that the patient does not convert within the maximum duration of the intensive phase applied by the programme. If no maximum duration is defined, an 8-month cut-off is proposed. For regimens without a clear distinction between intensive and continuation phases, a cut-off eight months after the start of treatment is suggested to determine when the criteria for Cured, Treatment completed and Treatment failed start to apply the terms 'conversion' and 'reversion' of culture as used here are defined as follows:

Conversion (to negative): Culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative Culture is used as the date of conversion.

Reversion (to positive): Culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining Treatment failure, reversion is considered only when it occurs in the continuation phase.

V. Case finding strategies

This entails identifying individuals who may be at a greater risk of developing drug-resistant TB compared to the general population and evaluating them appropriately using gene xpert, culture and DST. The following table illustrates these target group:

- All previously treated patients: a. failures ; b. relapses; c. treatment after loss to follow up
- DR TB contacts who have been diagnosed with active TB
- Healthcare workers with TB symptoms
- Patients who develop TB while on IPT
- Refugees with symptoms of TB
- Smear positive at 2 months of drug sensitive treatment
- Prisoners with TB symptoms

VI. Diagnosis of DR TB

Definitive diagnosis of drug-resistant TB requires the detection of Mycobacterium tuberculosis bacteria and determination of resistance to anti-TB drugs using gene xpert and culture and DST respectively.

Steps to follow you have identified a DR TB patient

1. **Inform** the SCTLC
2. Carry out thorough **patient history** and medical examination
   a. **Patient History**

      Take a detailed history of the patient:
      - Demographic data, residence, contact details of the patient and next of kin
      - Past medical history of TB treatment and outcome
      - HIV status
      - History of drug allergies, smoking, alcohol or any other drug use and comorbidities

   b. **Physical examination:** Carry out a head to toe examination and nutritional assessment
3. Provide **Psycho-social assessment** and health education to the patient
   i. The patient should identify a treatment supporter

Counseling tips for MDR-TB patients

Table 3.40: Counseling tips for MDR-TB patients

If the patient does not know what MDR-TB is	Explain that MDR-TB: • Is created when TB patients do not take anti-TB drugs regularly. • Is transmitted through the air. • Can be easily transmitted to people living with HIV.

If the patient does not understand MDR-TB treatment	Explain: • That second-line drugs are weaker than first-line Drugs, so it is important to take all doses on time. • That the injectable will be taken for at least eight months but this depends on culture conversion • That the total duration of treatment is at least 20 months and at least 18 months after culture Conversion.
If the patient is worried about adverse effects of MDR-TB treatment	Explain: "This treatment can have many side effects, especially at the beginning of treatment. If you are having any side effects, you should tell the community health worker immediately. Side effects get better with time."
If the patient has had difficulties adhering to treatment in the past	Explain: "It is very important for you to take all of your doses. Tell me about difficulties you have had with taking treatment in the past."
If the patient does not know his/her HIV Serostatus	Provide HIV counseling and offer HIV testing and treatment as per recommended guidelines.
If the patient lives with other family members	Explain: • Most infectious before starting treatment and during the first few weeks of treatment. • Leave windows and doors open in the home to increase ventilation, spend more time outdoors. • Don't sleep in the same bed as other family members during this time. • Practice cough etiquette
If the patient lives far from the clinic	Assess patients' willingness to be enrolled in a nearby facility for treatment.

4. **Take an informed consent** prior to initiation of treatment after explaining to the patient all the above i.e. what to expect during treatment, adherence, side effects and length of treatment.

5. **Prepare patient for MDR TB treatment**

a. Laboratory preparation

The following tests should be done:

i. Full hemogram
ii. Liver function test
iii. Renal function tests
iv. Pregnancy test
v. Thyroid function test
vi. CD4 count if HIV positive
vii. Sputum test
    i. Microscopy
    ii. Culture and sensitivity tests

b. Clinical test

i. Audiometry (hearing test)

ii. Chest XR

iii. ECG

c. HIV testing

- Counsel the patient on the need to know his/her status and test in line with the existing protocols.
- Initiate Cotrimoxazole and ART if HIV positive according to the guidelines
- Discuss the consequence of co infection and transmission prevention partner testing, cough etiquette and use of condoms

6. Carry out contact tracing of all DR TB contacts

- Screen patients for symptoms for TB
- Those found to have TB symptoms should have gene xpert, culture and DST and chest xray done
- Contacts should be screened every month during the intensive phase and every three month during the continuation phase
- Contacts should be screened for one year post treatment

7. Home Visit

- Prepare to visit the patient at home
- Assess the residence, number of rooms, number of people in the house, ventilation in the house
- Assess patient's physical movements e.g. to church, market and other congregate setting
- Screen the household contacts for TB using symptom screen
- Refer any symptomatic contacts to the nearest health facility for further screening
- Provide health education to household members

VII. Treatment of Drug Resistant Tuberculosis

Classes of anti TB drugs used in management of DR-TB

The drugs used are classified into 4 groups based on their efficacy, experience of use and drug class. These groups are shown in the table below.

Table 3.41: Drugs for treatment of Tuberculosis

Group A - Fluoroquinolones	Levofloxacin Moxifloxacin Gatifloxacin	Lfx Mfx Gfx

Group B - Second-line injectable agents	Amikacin Kanamycin Capreomycin	Am Km Cm
Group C - Other core second-line agents	Prothionamide Cycloserine Clofazimine Linezolid	Pto Cs Cfz Lzd
Group D - Add-on agents	**Group D1** Pyrazinamide Ethambutol High-Dose Isoniazid	 Z E H (high dose)
	Group D2 Delamanid Bedaquilline	 Dlm Bdq
	Group D3 p-amino-salicylic acid Meropenem/Imipenem* (+Amoxicillin/Clavulanate)	 PAS Ipm/Mpm (+Amx/Clv)

Kenya DR TB treatment regimen

Treatment of DR TB regimen in Kenya is based on the resistance pattern that is largely **standardized regimen** as recommended by WHO as shown below.

Pattern of Drug Resistance	Regimen	Duration
Isoniazid **and** Ethambutol **and** Pyrazinamide **±** streptomycin	3 Km-Lfx-R-Z/ 15 LFX-R-Z	15 months
Isoniazid **and** Pyrazinamide	3 Km-Lfx-R-Z/ 15 LFX-R-Z	15 months
Isoniazid **and** Ethambutol	3 Km-Lfx-R-Z/ 15 LFX-R-Z	15 months
Isoniazid ± Streptomycin	R/Z/E/Lfx	9 months

An **individualized regimen** is constituted based on results of Drug Susceptibility Testing (DST). This decision shall be made in consultation with the clinician, TB coordinators and the PMDT clinical team. Different resistant patterns will require unique treatment regimen as shown in the table below:

VIII. Shorter Term Regimen for Rifampicin Resistant TB

STANDARD OPERATING PROCEDURES FOR THE SHORTER MDR TB REGIMEN

THE SHORTER MDR TB REGIMEN

This is a shorter MDR TB regimen lasting 9 to 11 months. The intensive phase is 4 to 6 months while the continuation phase is 5 months.
Intensive phase: 4-6 months* **(**7 Drugs one of which is an injectable)

High dose Isoniazid** + Kanamycin + Ethambutol + Pyrazinamide + Moxifloxacin + Prothionamide + Clofazimine

Continuation phase: 5 months

Ethambutol + Pyrazinamide + Clofazimine + Moxifloxacin

*** Intensive phase duration is 4 months. However, this may be prolonged to 6 months depending on smear microscopy conversion**

**** Isoniazid is given at high doses based on weight**

Eligibility Criteria

This regimen is recommended for all patients with **rifampicin-resistant** tuberculosis **with or without** isoniazid resistance.

Exclusion Criteria

The following patients should be excluded from this regimen:

- Pregnant women
- Extra-pulmonary TB cases
- Confirmed resistance, to a medicine in the shorter MDR-TB regimen other than resistance to isoniazid
- Patients who have been exposed to **second line** medicines included in the shorter MDR-TB regimen for more than one month
- Intolerance to more than 1 medicine in the shorter MDR-TB regimen or increased risk of toxicity
- Known or potential for drug-drug interactions
- Close contacts to pre XDR/ XDR patients who present with signs and symptoms of TB

- **Patients who are excluded from using the shorter term regimen, should be initiated on the individualized regimen**
- **The National PMDT clinical team should be informed immediately such a patient is identified**

Whose sample do you send for second line DST?

All patients diagnosed with rifampicin resistance should have their sample sent to the National of Reference Laboratory for second line DST immediately this diagnosis is made.

Preparation of a patient for treatment

a. **Counsel patient on treatment and obtain an informed consent**
b. **Laboratory preparation**

The following laboratory investigations are mandatory before initiation of treatment:

- Full hemogram
- Liver function test-AST, ALT
- Renal function tests- Creatinine, Potassium
- Pregnancy test
- Thyroid function test- TSH
- Glucose
- Viral and CD4 count if HIV positive
- Sputum for:
  a. LPA for 1st and 2nd line DST
  b. Microscopy
  c. Culture

c. **Other investigations**
   i. Audiometry (hearing test)
   ii. Chest XR
   iii. ECG

NB: Baseline tests are mandatory

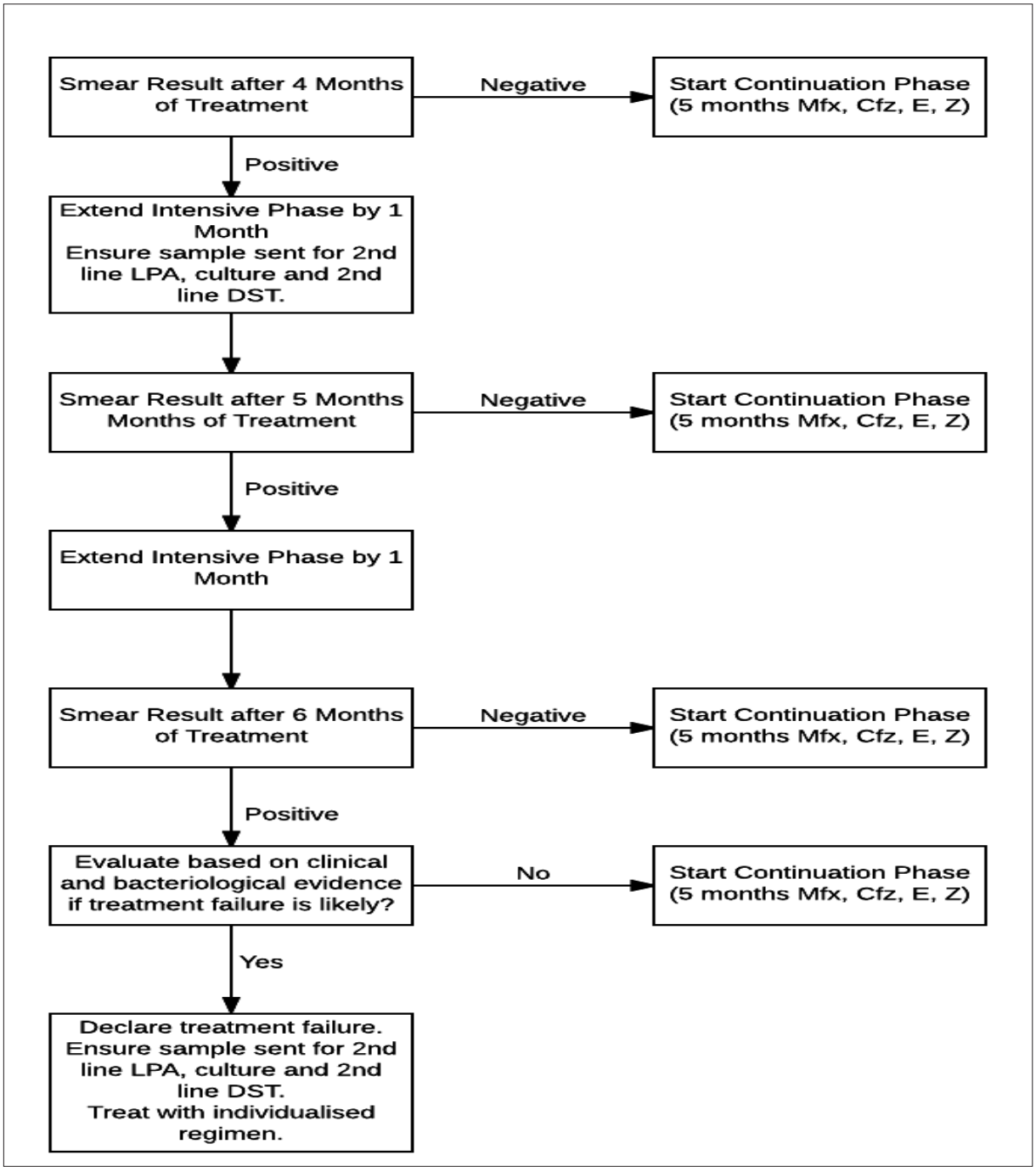
TREATMENT

Upon initiating a patient on treatment:

1. Intensive phase ends at the end of month 4
   a. It should be extended to a maximum of 6 months in cases of lack of smear conversion at 4 months
2. If intensive phase extends to month 6, ensure that the relevant investigations for monitoring are also conducted alongside
3. If cultures are positive at month 4 of treatment, ensure you repeat second line DST and monitor closely
4. If the patient remains smears positive at month 6 and/or is culture positive at 6 months, the patient will be declared as a treatment failure

5. Manage HIV positive patients as indicated in the National ART guidelines
6. Treatment should be strictly directly observed for the entire duration
7. Treatment should be initiated even as baseline laboratory results are being processed
8. Remember to revise and adjust dosages depending on the patient's' weight during the course of treatment
9. Second line DST results must be obtained. However, this should not delay patients from being initiated on treatment

Transition from the intensive phase to the continuation phase



Follow up and monitoring of patients on the Shorter Term Regimen

Month	Baseline	1	2	3	4	5	6	7	8	9	10	11
Clinical review	X	Every 2 weeks	X	X	X	X	X	X	X	X	X	X
Audiometry*	X	X	X	X	X							
Audiometry must be done monthly during intensive phase												
Weight	X	X	X	X	X	X	X	X	X	X	X	X
Height	X											
Smear	X	X	X	X	X	X	X	X	X	X	X	X
Culture	X	X	X	X	X	X	X	X	X	X	X	X
Sputum smear and culture must be carried out monthly until the end of treatment												
1st line DST	X											
2nd line DST	X				X		X					
LFTs (AST, ALT, Bilirubin)	X	X	X	X	X							
Creatinine Potassium, Magnesium	X	X	X	X	X							
Full Hemogram	X				X							X
Viral load	X						X					X
RBS	X											X
Pregnancy Test	X											X
CXR	X											X
TSH	X				X							X
ECG	X	Every 2 Weeks										

TREATMENT FAILURE

Suspect treatment failure when any of the following is present:

- Patient's' clinical condition deteriorates that is - weight loss or respiratory insufficiency
- Persistently positive cultures or smears past 6 months of treatment

  Worsening chest x-ray features
- Reversion of culture from negative to positive in the continuation phase
- Development of resistance to the injectable and/or fluoroquinolone at any time

Assessment of patients when treatment failure is suspected

1. A clinical management meeting should be convened urgently to discuss the patient
2. Review the treatment card and assess adherence to determine if the patient is receiving all the right drugs and doses
3. Assess for other illnesses or other comorbidities that may mimic features of treatment failure through clinical and chest radiographic deterioration that may occur together simultaneously with repeated culture- and smear-negative results.

   Certain conditions or diseases that may decrease absorption of medication such as chronic diarrhoea, immunosuppressive conditions, diabetes and malignancies, drug-drug interaction
4. Review previous bacteriological results
   a. One single positive culture in the presence of an otherwise good clinical response can be due to a laboratory contaminant or error
   b. Positive smears with negative cultures may be caused by the presence of dead bacilli and therefore may not indicate treatment failure
5. Review previous DST results
   a) If there is evidence of acquired resistance to fluoroquinolones or second line injectable drugs while on the STR regimen, treatment failure is probable
6. Collect sputum specimen for 2nd line DST to check for amplification of resistance
7. **DO NOT** add any drugs to the regimen

Declare treatment failure

After assessing for treatment failure and there is need for treatment termination or permanent regimen change of at least two anti-TB drugs because of:

- Lack of conversion by the end of the intensive phase
- Bacteriological reversion in the continuation phase after conversion to negative
- Evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs
- Adverse drug reactions

What to do when you declare treatment failure

Notify the National PMDT coordinator and discuss on the best individualized regimen with new molecules.

POST-TREATMENT FOLLOW UP

After treatment with the shorter term regimen, patients need to be evaluated for relapse at month(s) 3, 6 and 12 months after completion of treatment using signs and symptoms. If TB is suspected:

- Send sample to the National Referencce Laboratory for culture and 2nd line DST

  Do a chest xray

- Evaluate for other conditions
- Consider post TB sequalae

Shorter term MDR regimen (STR) under special circumstances:

- TB/HIV- Patients should be managed according to the standard National HIV guidelines.
- Diabetes- Monitor for peripheral neuropathy
- Patients who have skipped medicines for less than two months, continue treatment and add the doses missed
- If the patient has missed for more than 2 months transition to individualized treatment regimen.

Dosage of Medicines in the Shorter MDR-TB Regimen

Drug	Weight group		
	Less than 30 kg	30 kg to 50 kg	More than 50 kg
Gatifloxacin	400 mg	600 mg	800 mg
Moxifloxacin	400 mg	600 mg	800 mg
Clofazimine	50 mg	100 mg	100 mg
Ethambutol	800 mg	800 mg	1200 mg
Pyrazinamide	1000 mg	1500 mg	2000 mg
Isoniazid	300 mg	400 mg	600 mg
Prothionamide	250 mg	500 mg	750 mg
Kanamycin†	15 mg per kilogram body weight (maximum 1 g)		

†For adults over 59 years of age, the dose will be reduced to 10 mg/kg (max dose 750 mg).

Bedaquiline

Introduction

Bedaquiline belongs to a new class of drugs called diarylquinolines.
It plays a crucial role in strengthening a regimen when MDR TB patients have strains resistant to fluoroquinolones or second line injectable drugs.

Properties of Bedaquiline

- Bedaquiline works by targeting mycobacterial adenosine triphosphate (ATP) synthase that is essential for the supply of energy to *Mycobacterium tuberculosis* and most other mycobacteria.

- It has a strong bactericidal and sterilizing activity against *M. tuberculosis*.
- The drug has a 5½ months half-life
- Better absorption is obtained if taken with food

The dose of Bedaquiline

- Bedaquiline comes in 100 mg tablets
- It is only given for the first 24 weeks of treatment

The six-month dosing schedule of the medication is as follows:

Week	No. of tablets	Schedule
Week 1 and 2	4 tablets daily (400mg OD)	Seven days per week*
Week 3 to 24	2 tablets daily (200mg OD)	Three times per week (at least 48hrs between doses preferably Monday, Wednesday and Friday)**
Start of month 7*** – Marks the end of treatment	No bedaquiline	No bedaquiline

***If a dose is missed during the first two weeks of treatment, patients should not make up for the missed dose but should continue the usual dosing schedule and complete 14 days of the 400mg dose**

****From week 3-24 onwards, if a 200 mg dose is missed, patients should take the missed dose as soon as possible, and then resume the three times a week regimen** e.g. if a patient misses Monday, then the patient should take Tuesday, Wed and Friday.

*****If there is a delayed microbiological response (i.e the patient does not have sputum culture conversion by month 4), or the treatment regimen is compromised (i.e less than 4 effective drugs) - hold a clinical team to discuss the treatment regimen to consider prolonging the course of Bedaquilline. Involve the national clinical team in the review of such patients.**

Indications for Bedaquiline

1. Resistance to fluoroquinolones (Pre-XDR or XDR)
2. Resistance to second line injectables (and sensitivity to fluoroquinolones), as an alternative to delamanid
3. Severe adverse drug reactions (i.e hearing loss), poor tolerance or contraindications to any component of standardized regimen, as an alternative to delamanid
4. Contact with a patient with resistance to fluoroquinolones
5. Patients who are "treatment failure" of a MDR-TB regimen.

Patient selection

- Any adults (≥18 years old) with MDR-TB who meets any of the above indications
- Children (≥6 years old) should be treated with delamanid

Contraindications

1. Hypersensitivity. The patient is hypersensitive to the active substance or to any of the excipients in the formulation.
2. High risk for cardiac complications. Patient has a baseline QTc interval greater than 500 ms, history of torsades de pointes or cardiac ventricular arrhythmias or severe coronary artery disease.
3. Children or persons under 18 years of age. The safety and dosing of bedaquiline has not been established in children.
4. Pregnancy. The safety of this drug has not been established.
5. Nursing mothers.
    a. It is not known if bedaquiline and its metabolites are passed into human breast milk. Because of the potential for adverse reactions in nursing infants, a decision should be made on whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Saving Bedaquiline for only "the most resistant" patients or the "most desperate cases" may result in poor outcomes and is likely NOT the best way to maximize its benefits

Bdq should not be added alone to a failing regimen

Medicines Recommended for the Treatment of MDR

*** Carbapenems and clavulanate are meant to be used together; clavulanate is only available in formulations combined with amoxicillin**

Building an MDR Regimen with the New Drugs

1) Choose Bdq or Dlm based on indication
2) Choose a higher generation FQ if sensitive based on DST and treatment history
3) Choose a second-line injectable agent if sensitive based on DST and treatment history
4) Add at least two drugs from Group C that are likely effective based on treatment history
5) Add 1st line drugs from Group D1 that may still be effective
    a) Z is routinely added unless well founded reasons to believe there is resistance or there risk of toxicity
6) Add drugs in Group D3 until there are at least 5 drugs likely to be effective.

Patient Type	Example Regimen
MDR with intolerance/contraindication to SLID	Dlm (or Bdq)-Lfx-Pto-Cs-Cfz-Z
MDR with resistance to FQ (Pre-XDR)	Bdq (or Dlm)-Km-Pto-Cs-Cfz-Z
MDR with resistance to SLID (Pre-XDR)	Dlm (or Bdq)-Lfx-Pto-Cs-Cfz-Z
MDR with two Group C drugs (Pto and Cs) compromised	Dlm (or Bdq)-Lfx-Km-Cfz-Lzd-Z
XDR with Group C drugs (i.e Pto and Cs) compromised	Bdq or Dlm-Lzd-Cfz-Imp (+Amx/Clv)-Z

This is only a guide regimen but not a standardized regimen for use of bedaquiline or delamanid.

Points to remember:

1. The algorithms always maintain the principle of **never** using less than five drugs likely to be effective. If effectiveness is difficult to judge, the drug can be added to the regimen, but should not be counted as a core effective drug.
2. Do not add Bedaquiline to a failing regimen

Concomitant therapy in HIV-positive patients

- **NVP is considered the best option if using Bedaquilline**
- Efavirenze cannot be used with Bedaquilline as it **decreases** its concentration by almost 50%. It can however be used with Delamanid
- Protease Inhibitors (PI) will increase blood levels of Bedaquilline and Delamanid. If a PI is required,
- Delamanid is preferred over Bedaquilline.
- The following possibilities exist for patients with HIV/AIDS who need Bdq:
  - **If patient is not yet on ART:** Start on Bdq regimen and initiate NVP-based ART regardless of CD4 count
  - **If the patient is already on NVP** : Start on Bdq and continue with the NVP regimen
  - **If patient is on a lopinavir/ritonavir-based regimen:** Delamanid is preferred
  - **If patient is already on EFV:** Check viral load (VL)
    - If VL undetectable, stop EFV and start NVP for the duration patient will be on Bdq.
    - If VL detectable, consider ART failure. Stop EFV and start lopinavir/ritonavir-based second-line regimen and use Delamanid instead of Bedaquiline. Or consider the use of Raltegavir which can be used with Bedaquiline. Discuss with HIV clinic and National Clinical Team.

- **Be aware of potential additive hepatotoxicity with NVP and Bedaquiline**

If the bedaquiline is stopped in a patient on ART because of QT prolongation, the ART is often continued except if dangerous arrhythmias are present, in which case all QT prolonging drugs are stopped.

Drug interactions with Bedaquiline

- CYP3A4 inducers -rifamycins, EFV
- CYP3A4 inhibitors- ketoconazole, PI's
- QT prolonging drugs
    - Delamanid
    - FQs-Moxifloxacin, gatifloxacin
    - Clofazimine
    - Macrolides-erythromycin, clarithromycin
    - Azole antifungals-ketonazole, fluconazole
    - Antimalarials (quinine sulfate, chloroquine).
    - Antipsychotics (e.g. chlorpromazine, haloperidol)
    - ARVs

Monitoring and follow up of patients receiving Bedaquiline

Clinical and Laboratory Patient monitoring

Month	Baseline	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21
Clinical review	X	Every 2 weeks	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Audiometry	X	X	X	X	X	X	X	X	X							
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Smear	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly till treatment completion		
Culture	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly till treatment completion		
1st line DST	X						X									
2nd line DST	X			X			X									
LFTs (AST, ALT, Bilirubin)	X	X	X	X	X	X	X			X			X	X	X	
Creatinine Potassium, Magnesium	X	X	X	X	X	X	X	X	X							

Full Hemogram	X			X			X						X		X	
CD4	X						X						X		X	
RBS	X															
Pregnancy Test	X															
CXR	X						X						X		X	
TSH	X		X				X						X			
ECG	X	Every 2 weeks	X	X	X	X	X	X	X	X						

1. QT interval monitoring

- This is the most frequent adverse drug reaction (>10% of patients) occurring during treatment with Bedaquiline. A prolonged QT (QTc>500 is a risk factor for Torsades de Pointes.
- MDR-TB Drugs that cause QT prolongation: Bedaquiline, Delamanid, Moxifloxacin, Clofazimine.
- ECGs should be obtained at baseline, end of week 2, end of week 4 and monthly thereafter to monitor the QT interval during bedaquiline use.
- Do an ECG if the patient has clinical symptoms (tachycardia, syncope, palpitations, or weakness or dizziness) of cardiotoxicity.

Management of Prolonged QT Interval

PARAMETER	GRADE 1 (MILD)	GRADE 2 (MODERATE)	GRADE 3 (SEVERE)	GRADE 4 (LIFE THREATENING)
Prolonged QTc Interval	450-480 ms	480-500 ms	> 500 ms	> 500ms or >60 ms change from baseline and one of the following: torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia
Suggested Management	Monitor ECG weekly until QTc <450ms. Check electrolytes and replace as necessary.	Monitor ECG weekly until QTc <450ms. Check electrolytes and replace as necessary.	Stop QT prolonging drugs. Monitor ECG. Hospitalize and replace electrolytes as necessary.	Treat arrhythmia. Stop QT prolonging drugs. Monitor ECG. Hospitalize and replace electrolytes as necessary.

Suggested Management Strategy

- If cardiac symptoms such as **tachycardia, syncope, palpitations, weakness or dizziness** are present at any time while a patient is on Bedaquilline, obtain an ECG urgently to check the QT interval and rule out an arrhythmia.
- If QTc is >500ms, stop all QT prolonging drugs and hospitalize in a facility capable of managing arrhythmias.
- Check and replace electrolytes
    - If hypokalemia is present , urgently replace potassium and monitor as per the guidelines until normal levels are reached
    - If potassium is low, check magnesium and calcium and replace as needed. If unable to test, give oral magnesium and calcium empirically.
- Do TSH to exclude hypothyroidism

  Monitor ECGs at least weekly to confirm that the QT interval has returned to baseline.
    - Once stable (QTc<450 and electrolytes are normal) QT prolonging drugs can be added back to the regimen.
- Consult a cardiologist for multidisciplinary management of the patient as soon as possible.
- Given the long half-life of Bdq, addition of other drugs (i.e Dlm, Cfz) after Bdq is discontinued, can still result in cumulative QT prolongation.

2. Liver function monitoring

- MDR-TB Drugs that are more likely to cause hepatotoxicity are Pyrazinamide, Bedaquiline, Linezolid and Clofazimine
- Due to a high incidence of liver toxicity seen in patients on Bedaquiline, Liver enzymes should be monitored monthly.
- Stop All TB drugs if:
    - Aminotransferase (ALT/AST) elevations are >3 times upper limit of normal (ULN) and accompanied by total bilirubin elevation or symptoms/signs of liver failure (e.g encephalopathy) or
    - Aminotransferase elevations are >5 times the upper limit of normal (regardless of symptoms)
- When liver functions returns to normal, the patient has to be re-challenged (starting with the least hepatotoxic drug) to identify the responsible drug which should be stopped permanently.
- Rule out viral hepatitis
- Alcohol and other hepatotoxic drugs should be avoided while on bedaquiline

Caution

- Geriatric use (use in the elderly).
- Hepatic impairment. No dose adjustment is necessary for bedaquiline in patients with mild or moderate hepatic impairment.
- Renal impairment. No dose adjustment is required in patients with mild or moderate renal impairment.

- Concurrent use of delamanid: no data exist about concomitant use of delamanid and bedaquiline. Combination of delamanid and bedaquiline can be considered following approval by an expert committee where necessary.

Active pharmacovigilance measures must be in place to ensure early detection and proper management of adverse drug reactions and potential interactions with other drugs.

CLINICIAN'S CHECKLIST OF ESSENTIAL PARAMETERS FOR SELECTION OF MDR-TB PATIENTS WITH BEDAQUILINE

Patient is at least 18 years old.	Yes ____	No ____
Patient is known or suspected to be diseased with a multiple-resistant strain of tuberculosis and therefore eligible for treatment with second-line anti-TB drugs.	Yes ____	No____
Additional laboratory data has been obtained on the susceptibility profile of the patient's TB isolate to the following agents: fluoroquinolones (ofloxacin and moxifloxacin), and second-line parenteral agents (kanamycin, amikacin and capreomycin).	Yes____	No____
The drug resistance profile of the patient's isolate suggests that the WHO standard recommended regimen for treatment of MDR-TB cannot be provided.	Yes____	No_____
Clinically significant ventricular arrhythmia is absent.	Yes____	No_____
Baseline ECG shows normal QT interval	Yes____	No ____
Aminotransferase and total bilirubin within normal limits.	Yes ____	No____
The patient's serum potassium, calcium, and magnesium have been obtained at baseline and levels are within normal limits.	Yes____	No ___
Informed consent for treatment with bedaquiline has been obtained	Yes____	No____

If the answer is 'yes' to all questions, the patient can be enrolled on treatment with bedaquiline as per the algorithms.

If the answer is 'no' to any of the above, further consideration and review is needed before enrolment in a treatment regimen with bedaquiline. *

***Getting a 'no' response to any of the above is not an absolute contraindication to using bedaquiline, only that the situation should be reviewed and the risk benefit of bedaquiline be reconsidered under the circumstance**

Delamanid

Introduction

Delamanid belongs to a new class of drugs called Nitrodihydro-Imidazo-oxazole.
It is recommended to be added to the WHO-recommended longer regimen in children and adolescents (6 – 17 years) with multidrug- or rifampicin-resistant TB (MDR/RR-TB) who are not eligible for the shorter MDR-TB regimen.

Delamanid should be added to a multidrug backbone regimen in individuals who are at high risk of treatment failure, including those with extensive disease, diabetics, persons with HIV, and other populations with poor outcomes according to local program data.

Properties of Delamanid

- Delamanid is a Mycobacterial cell wall synthesis inhibitor
- The identified metabolites of Delamanid do not show anti-mycobacterial activity.
- Delamanid has a lower genetic barrier to develop resistance compared with Bedaquiline and Linezolid
- The drug has a 30-38 hours half-life
- Steady-state concentration is reached after 10-14 days
- Absorption is increased a standard meal a standard meal.
- Delamanid is not excreted in urine.
- No data are available regarding CNS penetration.
- Store tablet at room temperature and in original package.
- There is no known cross-resistance of Delamanid with any existing anti-TB drugs.

The dose of Delamanid

- **Children** (aged 6–12 years) -50 mg twice daily for 6 months
- **Adolescents** (aged 13–17 years) and **Adults** -100 mg twice daily for 6 months
- Delamanid comes as a 50mg coated tablet

Length of treatment of delamanid-containing regimens

Drug	Suggested duration of treatment (in months) when delamanid is added to the standard WHO regimenaNo. of tablets
Delamanid (oral) 6	6
Injectable drug	6–8
Other oral anti-TB drugs	20

Indications for Delamanid

Novel agent of choice in patients who have an indication for receiving a new TB drug based on second-line resistance or intolerance in the following populations:

1. Ages of 6 and above years

2. Individuals on antiretroviral therapy who cannot be changed from an efavirenz based regimen
3. Persons with a history of allergy, intolerance, or prior exposure to bedaquiline
4. Persons with > 1 month history of clofazimine treatment, as there are some early lab reports of cross resistance seen between bedaquiline and clofazimine
5. Pregnant women

Patient selection

- Adults (age ≥18 years) with pulmonary MDR-TB disease, including people living with HIV

Caution

- ≥ 65 years
- Diabetes
- Severe Hepatic impairment
- Alcohol or other substances
- Severe renal impairment

NB/ Use of the drug in children and in pregnant and breastfeeding women is not currently advised due to a lack of evidence on safety, efficacy and proper dosing in these groups**.**

- **Using Delamanid only in individuals who have "no other options" will not likely yield positive results.**
- **Delamanid is used together with other standard medicines. It must not be taken on its own.**

Constructing a Delamanid-containing regimen

Points to remember:

1. Delamanid should not be introduced into a regimen in which the other companion drugs are known or believed to be ineffective, or are failing to show effectiveness.
2. The algorithms always maintain the principle of never using less than four effective second-line drugs.
3. Group 5 drugs other than Delamanid are added based on the number of Group 4 drugs for which there is a high degree of confidence in efficacy:
    - Confidence in all three Group 4 drugs: adding other Group 5 drugs is not necessary.
    - Confidence in only two Group 4 drugs: add one other Group 5 drug.
    - Confidence in only one Group 4 drugs: add two other Group 5 drugs.
    - Confidence in no Group 4 drugs: add three other Group 5 drugs.
4. Avoid moxifloxacin when using delamanid.
5. Avoid Bedaquiline as an additional group 5

SCENARIO 1: MDR-TB plus evidence of (or unknown) susceptibility to Groups 2 and 3 agents and with risk of poor treatment outcome

An injectable Kanamycin/ Amikacin/ Capreomycin

Plus

Levofloxacin

Plus

Levofloxacin

Plus

Cycloserine/terizidone

Ethionamide/prothionamide,

Para-aminosalicylic acid (PAS)

(Use at least two Group 4 drugs thought to be effective).

Plus

Pyrazinamide/ Ethambutol

Plus

Delamanid and other Group 5 drugs as necessary

SCENARIO 2: MDR-TB plus resistance to fluoroquinolones with no injectable resistance

An injectable Kanamycin/ Amikacin/ Capreomycin

Plus

Levofloxacin

Plus

Ethionamide/prothionamide

Cycloserine/terizidone

Para-aminosalicylic acid (PAS)

(Use all drugs thought to be effective).

Plus

Pyrazinamide / Ethambutol

Plus

Delamanid and other Group 5 drugs as necessary

SCENARIO 3: MDR-TB plus resistance or severe intolerance to all second-line injectable agents

An injectable Kanamycin/ Amikacin/ Capreomycin

Plus

Fluoroquinolone

Plus

Ethionamide/Prothionamide or Cycloserine/Terizidone or Para-aminosalicylic acid (PAS)
(Add all Group 4 drugs thought to be effective).

Plus

Pyrazinamide /Ethambutol

Plus

Delamanid and other Group 5 drugs as necessary

SCENARIO 4: MDR-TB plus two or more Group 4 drugs compromised (Group 2 and 3 drugs effective)

Injectable Kanamycin/ Amikacin/ Capreomycin

Plus

fluoroquinolone

Plus

Ethionamide/Prothionamide

Cycloserine/Terizidone

Para-aminosalicylic acid (PAS)

(Add the Group 4 drug thought to be effective).

Plus

Pyrazinamide/ Ethambutol

Plus

Delamanid and other Group 5 drugs as necessary

SCENARIO 5: XDR-TB

An injectable Kanamycin/ Amikacin/ Capreomycin

- If patient's strain is still susceptible to one of the injectable drugs, include in the regimen.
- If resistant to all injectable agents, consider not using any injectable or using one that the patient has never received based on clinical judgement

Plus

Fluoroquinolone

- If only ofloxacin DST is known (and resistant) use levofloxacin unless thought to be compromised (previous use in failing regimen or known contact with a patient with levofloxacin resistance).
- If resistance has specifically been shown to ofloxacin and/or levofloxaxin, and moxifloxacin DST is susceptible, consider adding moxifloxacin to the regimen.
- Use of the combination of moxifloxacin with delamanid and clofazimine (three drugs that strongly prolong the QT interval) should be avoided.
- If resistance shown to all three Group 3 agents, do not use fluoroquinolones.

Plus

Ethionamide/Prothionamide

Cycloserine/Terizidone

Para-aminosalicylic acid (PAS)

(Add all Group 4 drugs thought to be effective).

Plus

Pyrazinamide/ Ethambutol

Plus

Delamanid and other Group 5 drugs

Concomitant therapy in HIV-positive patients

- No dose adjustments are needed when delamanid is used with any of these antiretroviral agents
- Monthly monitoring with ECGs may be particularly important while on ART, especially with ritonavir-containing regimens.
- Non-protease inhibitor-containing regimens are the preferred ART when that option exists.

If the Delamanid is stopped in a patient on ART because of QT prolongation, the ART in often continued except if dangerous arrhythmias are present, then all QT prolonging drugs are stopped.

Overlapping toxicities:

Potential overlapping toxicities should be considered when Delamanid is used together with other second-line anti-TB drugs, ART, or other medications. Particular attention should be paid to concurrent use of Delamanid with drugs that prolong the QT interval.

Monitoring and managing patients receiving Delamanid

QT interval monitoring

Use of ECGs and active pharmacovigilance practices.

- ECG measurements are taken before treatment with Delamanid is started, and regularly during its use (ECG machines that directly report the QTc interval).
- Screening: ECG testing at baseline, weeks 2, 4, 8, 12 and 24 for Delamanid regimen and monthly if taking other QT prolonging drugs
- A value of greater than 450ms (males) or 470ms (females) is considered prolonged.
- If a patient taking Delamanid has a QTcF value of greater than 480 ms (or an increase of greater than 60 ms from baseline) on his or her ECG, electrolyte testing and more frequent ECG monitoring should be performed.
- A QTcF interval of more than 500 ms - stop the use of Delamanid and all other QT prolonging drugs in the regimen.

Liver function test

Delamanid is contraindicated in patients with albumin <2.8 g/dl.

Albumin levels should be obtained at baseline and corrected if abnormal by creating a positive nitrogen balance through enteral protein feeding.

Reversal of the inflammatory state during treatment for TB should also naturally lead to the normalization of serum albumin levels.

Weekly monitoring for patients with serum albumin between 2.9–3.4 g/ dl or experience a fall in serum albumin into this range during treatment

Electrolytes

Check K+, mg++ and ionized Ca++ and correct levels if found to be abnormal and withhold Delamanid and injectable agent (if still on it) until the electrolytes have normalized;
Monitor ECGs at least weekly to confirm that the QT interval has returned to baseline.
Repeat weekly ECGs to confirm that QTcF interval is stable.

Adverse drug reactions (>10.0% of patients)

- Nausea (38%)
- Vomiting (33%)
- Dizziness (30%).
- Others include anxiety, paraesthesia, and tremor.

General monitoring and management of these and other common adverse effects experienced by patients receiving second-line anti-TB drugs and also apply to patients receiving Delamanid. This includes monitoring the bacteriological and clinical responses

Drug interactions with Delamanid

- Strong inducers of CYP3A4 such as rifamycins (e.g. rifampin).
- QT prolonging drugs
    - Fluoroquinolones
    - Clofazimine
    - Moxifloxacin
    - ARVs-ritonavir containing regimens
    - Macrolide antibacterial drugs (erythromycin, clarithromycin, azithromycin).
    - Serotonin 5-HT3 receptor antagonist (such as ondansetron, an anti-nausea drug commonly used in MDR-TB).
    - Azole antifungal agents (e.g. ketonazole, itraconzaole, fluconazole). • Some antimalarials (e.g. quinine sulfate, chloroquine).
    - Some medicines to treat psychiatric disorders (e.g. chlorpromazine, haloperidol, thioridazine).

If possible, avoid the use of QT-prolonging drugs with delamanid. If it is absolutely necessary to include a QT-prolonging drug, increase ECG monitoring as described in

Drugs that lower electrolytes (i.e. injectable agents) can result in a higher potential for arrhythmias (including sudden death) due to QT prolongation, added electrolyte monitoring

Contraindications

Absolute contraindications:

- Patient refuses to consent.
- Hypersensitivity to the active substance or to any of the excipients in the formulation
- High risk for cardiac complications. Patient has a QT interval >500 ms, history of *torsade de pointes* or cardiac ventricular arrhythmias or severe coronary artery disease.
- Severe liver disease- Serum albumin <2.8 g/dL
- Severe renal disease.

Relative contraindications (with more frequent ECG monitoring and evaluation of risk versus benefit):

- Children or persons under 18 years old.
- Pregnancy
- Nursing mothers.
- Use with other QT prolonging drugs (see drug interactions).

Caution

- Use with caution in patients sensitive to lactose.

CLINICIAN CHECKLIST OF ESSENTIAL PARAMETERS FOR SELECTION OF MDR-TB PATIENTS ELIGIBLE FOR TREATMENT WITH DELAMANID (Tick Yes or No)

Patient is at least 18 years old. Yes____ No_____

Patient is known or suspected to be diseased with a multidrug resistant strain of tuberculosis and therefore eligible for treatment with second-line anti-TB drugs. Yes____ No_____

Additional laboratory data has been obtained on the susceptibility profile of the patient's TB isolate to the following agents: fluoroquinolones (ofloxacin and moxifloxacin), and second-line parenteral agents (kanamycin, amikacin, and capreomycin). Yes____ No_____

Clinically significant ventricular arrhythmia is absent. Yes____ No_____

Baseline and repeat ECG shows normal QT interval. Yes____ No_____

The patient's serum albumin, potassium, calcium and magnesium have been obtained at baseline and levels are within normal limits. Yes____ No____

• Due process for consent for treatment with delamanid has been followed ¨YES.. NO

If the answer is 'yes' to all questions, the patient can be enrolled on treatment with delamanid as per the algorithms in figures A4.1.1–A4.1.4.

If the answer is 'no' to any of the above, further consideration and review is needed before enrolment in a treatment regimen with delamanid.

Getting a 'no' response to any of the above is not an absolute contraindication to using delamanid, only that the situation should be reviewed and the risk benefit of delamanid be reconsidered under the circumstance.

IX. Extensively Drug-Resistant Tuberculosis (XDR-TB)

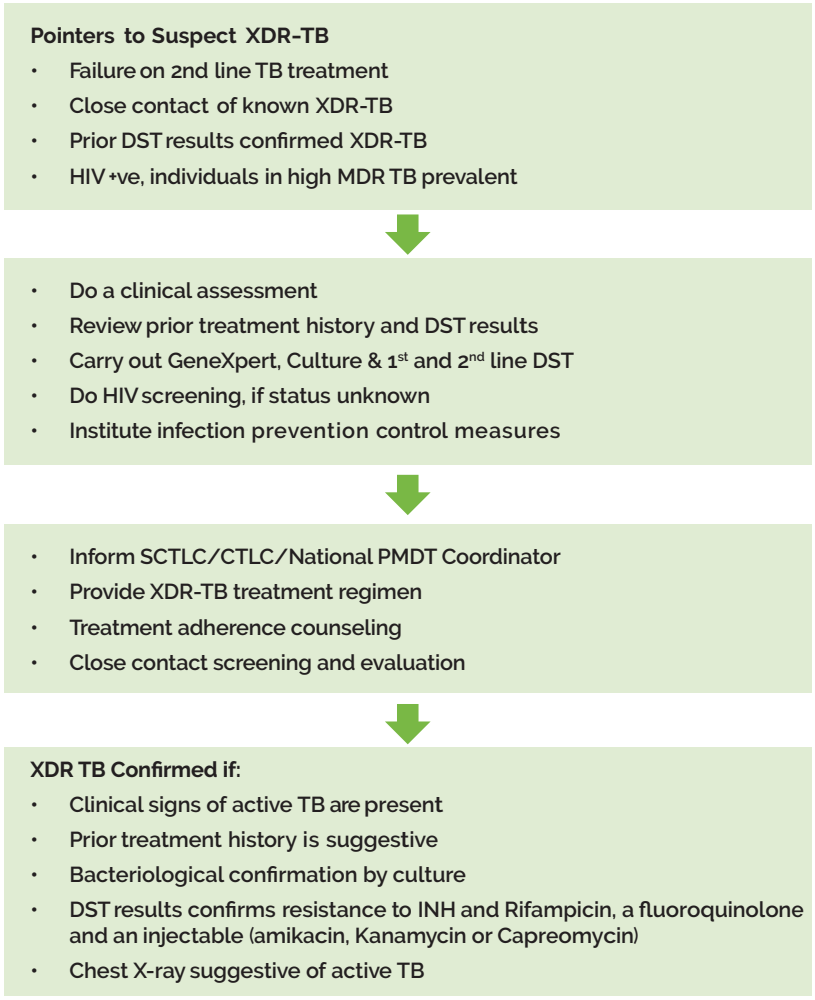
XDR-TB is a public health emergency that requires prompt diagnosis and treatment, appropriate isolation, and aggressive contact tracing. While cure rates for XDR-TB are lower than for MDR-TB, XDR-TB is a curable disease.

- All XDR-TB patients should receive an individualized treatment regimen based on the second line DST results.
- An effective regimen should contain at least five effective drugs. The regimen should include an injectable agent, a higher generation Fluoroquinolone, and drugs from Groups 1, 4 and 5 to which the isolate is known or suspected to be susceptible.
- Bedaquiline and Delaminid should only be used after receiving guidance from the National DR TB clinical team. (Annex Bedaquillin, Delaminid).

Indications for Bedaquilline and Delaminid

- Presumptive XDR and XDR
- In MDR TB, when group 4 drugs : Ethionamide or Prothionamide or Cycloserine and PAS drugs are compromised or severely toxic
- Severe intolerance to second line injectable
- Contraindications to other drugs

Figure 3.9: Management of a Suspected XDR TB Case



2ND LINE DRUGS AND DOSAGES

Table 3.43: 2nd Line drugs and dosages

Drugs	Weight Class			
	Average daily dosing	33-50kg	51-70kg	>70kg
Isoniazid (H) (100,300 MG)	10-20 mg/kg daily	200 - 300 mg daily	300mg daily or	300mg
Rifampicin ® (150, 300m mg)	10-20 mg/kg daily	450-600 mg	600 mg	600 mg
Ethambutol (E) (100, 400 mg)	25 mg/kg daily	800-1200 mg	1200-1600 mg	1600-2000 mg
Pyrazinamide (Z) (500 mg)	30-40 mg/kg daily	1000-1750 mg	1750-2000 mg	2000-2500 mg
Streptomycin (S) (1 G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Kanamycin Km (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Amikacin (AM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Capreomycin (CM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Ofloxacin (Ofx) (200,300,400mg)	The usual adult dose for MDR-TB is 800 mg	800 mg	800 mg	800-1000 mg
Levofloxacin (LFX) (250,500 mg)	The usual adult dose for MDR-TB is 750 mg	750 mg	750 mg	750-1000 mg
Moxifloxacin (Mfx)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Gatifloxacin (Gfx) (400 mg)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Ethionamide (Eto) (250 MG)	.15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Prothionamide (Pto) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Cycloserine (Cs) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Terizidone (Trd) (300 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
PAS 4gm sachets	150mg/kg daily	8gm	8gm	8-12gm
Pyridoxine (50mg)	For every 250 mg of Cycloserine, give 50 mg of Pyridoxine. Maximum dose of 200 mg			

- **Remember to revise and adjust dosages upwards or downwards depending on the patient's weight during the course of treatment.**
- **Second line drugs should be given once daily except for group 4 which can be given twice in case of adverse drug reactions. All doses should be observed by a health care worker and confirmed as swallowed.**
- **The minimum duration of intensive phase is 8 months until three consecutive negative cultures taken 30 days apart are obtained. This is equivalent to 4 months after culture conversion. Switch to continuation phase only when three most recent consecutive culture results taken at least 30 days apart, remain culture negative during the intensive phase.**

X. Monitoring and treatment follow up

Close monitoring of patients throughout the treatment period is important to evaluate clinical and bacteriological progress and any emergence of adverse drug effects and appropriate actions taken. There are essentially three components to treatment monitoring namely, clinical, laboratory and adherence:

Table 3.44: Monitoring

Monitor	Recommended frequency
Clinician	**During the intensive phase**: Every day if hospitalized and at least every week if treated as outpatient, until the treatment is well tolerated. **During the continuation phase**: Monthly assessments unless there is a medical necessity to see the patient more often.
DOT worker	At every DOT encounter, the supporter sees the patient daily between consultations and signals any concerns to the clinician.
Multi-disciplinary clinical team	Reviews patients at before initiating treatment and monthly till treatment completion
Weight	At baseline and monthly. Calculate BMI monthly for adults and Z scores for children.
Heights	At the start treatment for all patients. Repeat monthly for children.
Sputum smear and cultures	**MUST** be done at baseline and repeated every month until the end of treatment.
Audiometry	**At baseline**, then monthly during the intensive phase. Assess for symptomatic hearing loss during all clinic visits.

1st Line DST	At baseline and at month 6. This should also be done anytime there is a positive culture in a previously culture negative case.
2nd Line DST	2nd line DST should be done for all MDR TB patients at diagnosis, month 3 and 6 and if culture negative patient turns culture positive.
CXR	At baseline and then every 6 months until the end of treatment
Hemogram	At baseline then at month 3 and 6, then 6 monthly (or when necessary).HIV positive patients on AZT doe on month 4, 8, 12.
Serum Creatinine	At baseline then monthly while on injectable drug (and anytime it is clinically indicated)
Serum potassium, Magnesium	At baseline, then one week, then monthly while on the injectable agent (or when necessary)
Serum calcium & magnesium	At baseline then monthly while on the injectable agent (or when necessary)
TSH	At baseline, 3 and 6 months, then 6 monthly if on Ethionamide/ Prothionamide / PAS.
	If hypothyroidism is present then monitor monthly treatment completion.
LFTs (AST, ALT, Bilirubin)	At baseline, then month 1, 2, 3. Repeat every three months until treatment completion if on Pyrazinamide. And any time it is clinically indicated.
HIV screening	At baseline and if clinically indicated
Pregnancy test	At baseline for women of child bearing age; repeat if indicated.
RBS	At baseline, repeat if clinically indicated

Patients with mono and poly drug resistance to other drugs **EXCEPT** Rifampicin, should have GeneXpert done at month 2 and 3.

Note: The Use of GeneXpert in month 2 and 3 is to detect Rifampicin Resistance and not for monitoring response to treatment or follow up.

Table 3.45: Laboratory and Clinical Follow up for patients on treatment for MDR TB and HIV

Month	Baseline	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21
Clinical review	X	Every 2 weeks	X	X	X	X	X	X	X	X	X	X	X	X	X	**X**
Audiometry	X	X	X	X	X	X	X	X	X							
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Smear	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly till treatment completion		
Culture	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly till treatment completion		
1st line DST	X															
2nd line DST	X			X												
LFTs (AST, ALT, Bilirubin)	X	X	X	X			X			X			X	X	X	
Creatinine Potassium, Magnesium	X	X	X	X	X	X	X	X	X							
Full Hemogram	X			X			X						X		X	
CD4	X						X						X		X	
RBS	X															
Pregnancy Test	X															
CXR	X						X						X		X	
TSH	X		X				X						X			

Treatment delivery and adherence

During the intensive phase of DR-TB treatment, therapy will mostly be delivered in a hospital/ clinic setting (the DR-TB treatment centre) because of the need for daily injections. However it is possible to deliver the same treatment at home through community nurses, a treatment delivery mechanism that may reduce the risk of hospital transmission of DR-TB .

XI. Models of Drug Resistant TB Care and Treatment

- Isolation
- Facility based
- Community based

Criteria for selecting model of care of treatment

Table 3.46: Criteria for selecting model of care of treatment

Isolation	Facility based	Community based
• Preferred for refugees • Complications necessitating admission e.g. for blood transfusion, electrolyte imbalance etc. • XDR-TB • Mobile populations / Nomadic • Non-adherence	• Patient preference • Distance home patient – health facility < 5 km • Time to reach the health facility is < 1-2 hours • General condition of the patient is stable	• Patient preference • Distance home patient – health facility > 5 km • Time to reach the health facility > 1-2 hours • General condition of the patient is stable

PDR patients who need hospitalization should be isolated separate from the MDR TB -patients. XDR-TB patients **SHOULD NOT** be mixed with MDR, PDR, or other TB patients.

DR TB Clinical teams

Clinical teams will be established at the County and Sub-County levels and they will be responsible for managing DR TB patients in those regions.

The team is composed of the County TB coordinator, Clinician (Physician/M.O), Sub county TB coordinator, Pharmacist, DOT Nurse, Social worker, Public health officer, Lab technologist, Nutritionist, Community Health Extension Worker

The Sub County TB coordinator is the focal person to convene the monthly meetings with 3 or more members. Partners managing DR TB should send a representative to the clinical team meetings.

The Sub County TB coordinator is also expected to review all DR TB patients during the routine monthly supervision.

Roles

- Overall responsibility of managing DR TB in their regions
- Recommend initiation of DR TB treatment
- Carry out follow up of DR TB patients on treatment
- Reviewing all laboratory results including DST and culture of DR TB suspects and patients on treatment
- Reviewing complex cases as need arises e.g. adverse drug effects, co-morbidities and recommending appropriate interventions

- Co-ordinate referrals of DR TB patients to and from their counties
- Ensuring adequate and consistent commodity supply in their regions

Treatment Adherence

It is important to understand that many patients with MDR-B may have been non-adherent to previous treatment and could become non-adherent to current treatment if not strongly supported. To prevent non adherence and default from treatment the following measures are essential:

i. **Education/ counselling of patients**
All patients with MDR-TB and their families should receive education and counselling about MDRTB, its treatment, duration, potential adverse drug effects and the need for adherence to treatment throughout the period of treatment.

ii. **Assessment for risk factors for non-adherence**
All patient must be assessed for risk factors for non-adherence to treatment, including poor social circumstances (e.g. severe poverty or homelessness), drug and alcohol abuse, nutritional barriers (lack of food), non-facilitatory work schedules, drug adverse effects, denial of disease state and other adherence barriers including distances from health delivery points. Any identified factor(s) that may impact on adherence should be addressed. This may include the provision of incentives and enablers including food, shelter, transport, and psychological support (counselling and peer support).

iii. **Direct Observation of Therapy (DOT):**
All doses of MDR-TB medicines will be directly observed by HCW (DOTS-plus). The choice of DOT observer should be agreed with the patient and or his/her family. The DOT observer may be a health care worker or a community volunteer who should make every effort to accord the patient respect and dignity and maintain confidentiality. DOT providers/observer should receive appropriate training on DR-TB treatment and side effects, TB infection prevention control and the importance of adherence.

iv. **Default Retrieval**
A DOT register should be maintained in every centre treating MDR-TB patients. Every effort should be made to trace patients who miss a dose or scheduled appointment through the following interventions:

- Engaging the social workers, community health care workers and volunteers on tracing and discuss factors that could have led the patient to default.
- Carry out home visits to identify factors that may intefere with treatment.
- Interview the patient to identify medical or social factors that may have led to disruption of treatment

MDR and XDR TB Treatment failures

While treating MDRTB, some unfavourable outcomes are anticipated, including treatment failures and the presence of extensively drug resistant TB (XDR TB). Suspect treatment failure (except when there are Adverse drug reactions) when any of the following is present:

- Patient's clinical condition deteriorates that is - weight loss and respiratory insufficiency despite being on treatment.
- Persistently positive cultures or smears past 6 months of treatment
- Progressive, extensive and bilateral lung damage confirmed on X-Ray with no option for surgery.
- Reversion to culture or smear positive after they have been negative

When this happens**,** the following steps are recommended:

1. Review the treatment card and assess adherence to determine if the patient is receiving all the right drugs and doses.
2. Review all DST reports to determine the adequacy of the regimen and consider an alternative regimen where possible.
3. Repeat 1st and 2nd line DST to look for resistance amplification.
4. A clinical management meeting should be convened urgently to discuss the patient.
5. **DO NOT** add any drugs to the failing regimen. This decision will be made by the clinical team.
6. Look for other illnesses that may decrease absorption of medication (like chronic diarrhoea) or may result in immune-suppression (like HIV), diabetes and malignancies.

- Patients may have a positive smear with negative cultures that may be caused by the presence of dead bacilli and hence does not necessarily indicate treatment failure. Discuss such cases with the DR-TB clinical management team.
- In patients with repeated negative culture and smear results and no corresponding clinical and radiological improvement, then consider other diseases other than MDR-TB.

Suspending Therapy:

Treatment should be suspended when it is confirmed that all the drugs have been administered and there is no possibility of adding other drugs or carrying out any surgical intervention. At this point, supportive care regimen is considered.

The 2 most important considerations to suspend therapy and consider supportive care are:

- Patient's quality of life: continued use of the failing regimen can cause additional suffering without any benefits
- Public health concern**:** Continuing with the failing regimen can amplify resistance in the patient's strain and hence subsequent infection in the public.

This decision to suspend treatment should be made by the MDR-TB management team. Prepare the supportive care plan for the patient after consensus with the patient and the family members. This may include pain relief, management of respiratory insufficiency, nutritional support, and regular medical visits-particularly psychosocial support, home nursing care,

prevention and infection control measures as these patients normally remain infectious for a long time.

XII. Treatment of Drug Resistant TB in Special Conditions

Drug resistant TB may coexist with any number of medical problems and thereby present clinical challenges in the management of both diseases.

Contacts of DR TB

Treatment for contacts of MDR-TB patients

- Active contact tracing for all household and other close contacts of an MDR or XDR patient for clinical evaluation of signs and symptoms of TB disease.
- If signs and symptoms are present, a chest X-ray should be performed and sputum sample collected for GeneXpert, culture, DST and HIV counselling and testing. Young children and HIV-positive contacts should receive a chest X-ray even if they are asymptomatic.
- In areas where rapid DST testing is not immediately available, the contact patient should receive empiric second-line treatment based on the DST result of the index case. Adjust the regimen according to the DST results in consultation with the clinical team.
- MDR-TB should be suspected in children with active TB and having a close contact of an MDR-TB adult or an adult suspected to have died of TB or if they have bacteriological proven tuberculosis that is not responding to 1st line TB treatment.

Currently, **WHO does not recommend** any use of 2nd line drugs for chemoprophylaxis in MDR-TB contacts

DR TB in Children

Children with MDR or XDR TB have primary disease transmitted from a source adult case.

Suspect DR TB in children when:

- Is a contact with a known DR TB patient
- Is a contact with suspected DR TB who the source case is :
  - a treatment failure
  - retreatment case
  - recently died from TB
- A child with TB not responding to 1st line therapy despite adherence
- A child previously treated for TB present with recurrent disease.
- If the community in which the child resides (or had resided) has a high prevalence of drug-resistant tuberculosis.

Diagnosis of DR TB in Children

Every effort should be made to confirm drug resistant TB by culture and DST in children. However, children with active TB may be smear and culture negative posing a challenge in confirming a diagnosis of MDR or XDR.

Children with active TB who are household contacts of a confirmed MDR-TB or XDR-TB patient should be considered to have DR-TB, even if smear and culture are negative.

Treatment of DR TB in Children

- The child's treatment should be guided by the DST results.
- The regimen used to treat childhood drug resistant TB is similar to that used in adults.
- In children for whom DST results are not available, the DST pattern may be assumed to be similar to that of the contact.
- Empiric treatment for DR-TB should be initiated promptly, using a regimen based on the resistance pattern of the source case.
- Drug dosages should be based on body weight and the higher end of recommended range.
- Weights and Z-score should be measured monthly and dose adjustments made as the child's weight changes.
- In culture-negative children with DR-TB, clinical criteria can be used to determine response to therapy and the duration of the intensive and continuation phases.
- The DR-TB clinical teams should be involved in decisions made about paediatric cases.
- The benefit of fluoroquinolone far outweighs the risk, and should be part of every DR-TB regimen.

MDR-TB in Pregnancy

- Do a pregnancy test for all female patients of child bearing with MDR-TB prior to initiating treatment.
- An appropriate birth control method for all non-pregnant female patients should be provided during treatment.
- If pregnant, evaluate gestational age and severity of the drug-resistant TB.
- Discuss the risks and benefits of treatment should be carefully considered, with the primary goal of smear conversion to protect the health of the mother and child, both before and after birth. The following are some general guidelines;
    - Start treatment of drug resistance in second trimester or sooner if condition of patient is severe. Since the majority of teratogenic effects occur in the first trimester, therapy may be delayed until the second trimester. The decision to postpone the start of treatment should be agreed by both patient and doctor after analysis of the risks and benefits
    - Avoid injectable agents. For the most part, aminoglycosides should not be used in the regimens of pregnant patients and can be particularly toxic to the developing foetal ear. Capreomycin may carry the same risk of ototoxicity but is the injectable drug of choice if an injectable agent cannot be avoided.

- Avoid Ethionamide. Ethionamide/Prothionamide can increase the risk of nausea and vomiting associated with pregnancy, and teratogenic effects have been observed in animal studies. If possible, Ethionamide should be avoided in pregnant patients. PAS can be used as an alternative.

Caution: Rifampicin, protease inhibitors, some second-line MDRTB drugs, reduce the effectiveness of intradermal implanted contraceptives. Patients should be counselled to use alternative methods such as condoms, Depo-Provera, while taking these medications to avoid accidental pregnancy.

Pregnancy is not a contraindication for treatment of active drug-resistant TB.

DR TB and Breastfeeding

- Breastfeeding mothers should receive full course of DR TB treatment
- Infant formula shoud be substituted for breastmilk because small quantities of the drugs will be passed into the milk
- Clinicians and parents should agree to breastfeeding when the formula is not a feasible option
- The mother and her baby should not be completely separated.
- The care of the infant should be left to family members if the mother is sputum smear positive until she becomes sputum smear negative.
- The mother should be provided with an N-95 respirator if close infant – mother contact cannot be avoided. In the absence of an N-95 mask, the mother should be provided with a surgical mask until she converts.

DR TB and Diabetes mellitus

- Diabetes must be managed closely throughout the treatment of drug-resistant TB.
- Diabetes mellitus may potentiate the adverse effects of anti-TB drugs, especially renal dysfunction and peripheral neuropathy.
- Ethionamide or prothionamide may make it more difficult to control insulin levels hence may require the patient to increase the dosage as the use of insulin.
- **Medical follow-up**: Diabetes must be managed closely throughout treatment through a multidisplinary team every month.
- **Patient education:** The basics on the diet, treatment compliance, weight control, exercise, and foot care should be communicated to the patients, together with the symptoms of hypo- and hyper-glycaemia and what to do when they occur.
- **Creatinine and potassium** should be monitored weekly for the first month and then at least monthly thereafter because the injectables cause nephrotoxicity. For deranged results, seek physician.
- **HbA1C** should be monitored every six months if treatment changes or patient is not meeting target; every six months if stable.

- **Should be managed as pet the TB/HIV guidelines**

DR TB and Renal Insufficiency

Great care should be taken in the administration of second-line drugs in patients with renal insufficiency, and the dose and/or the interval between dosing should be adjusted for patients with a renal clearance of < 30 ml/ min or on haemodialysis. Table 5 below show the necessary Adjustment of ant tuberculosis medication in renal insufficiency

DR TB patients in Refugee Camps

The same guidelines have to be used in terms of treatment regimens. Onsite treatment has to be made available. Entire treatment should be coordinated by NTLD -UNIT. Should the camp close, NTLD -UNIT, IOM/UNHCR shall ensure continuation of treatment.

DR TB in Cross Border Patients

There is a need to establish cross border initiatives to facilitate treatment of patients that seek treatment in a neighbouring country. MDR TB among the refugee populations within Kenya will be managed in the refugee camps as per the National guidelines.

DR-TB and HIV co-infection

When a patient is newly diagnosed with both HIV and MDR-TB, the MDR-TB regimen should be started first. Cotrimoxazole and fluconazole prophylaxis if needed should be started together with the start of the MDR regimen. ARVs should be initiated 2-8 weeks after starting DR-TB treatment irrespective of the CD4 count. For patients receiving Rifampicin (i.e., Polydrug resistance), nevirapine should be avoided. The preferred regimens are AZT/3TC/EFV or ABC/3TC/EFV. If TDF is given in the intensive phase of MDRTB treatment, monitor regularly Creatinine levels due to potential additive nephrotoxic side effects with the injectable.

DR TB and Liver Disorders

Pyrazinamide is the most hepatotoxicity of the three first-line drugs: Rifampicin, isoniazid and pyrazinamide. Among the second-line drugs, Ethionamide, Prothionamide and PAS can also be hepatotoxicity, although less so than any of the first-line drugs. Hepatitis occurs rarely with the flouroquinolones.

Patients with a history of liver disease can receive the usual drug-resistant TB chemotherapy regimens provided there is no clinical evidence of chronic liver disease, hepatitis virus carriage, past history of acute hepatitis or excessive alcohol consumption. However, hepatotoxicity reactions to ant tuberculosis drugs may be more common in these patients and should be anticipated.

In general, patients with chronic liver disease should not receive Pyrazinamide. All other drugs can be used, but close monitoring of liver enzymes is advised. If significant aggravation of liver inflammation occurs, the drugs responsible may have to be stopped. If liver enzymes are elevated but less than 5 times normal, continue anti-TB therapy but follow liver function

tests each week. However, if liver enzymes greater than 5 times normal stop all anti-TB medications and repeat liver function tests weekly. Re- introduced the treatment once the LFTs are normal.

Uncommonly, a patient with TB may have concurrent acute hepatitis that is unrelated to TB or anti tuberculosis treatment. In this case, clinical judgement is necessary. In some cases, it is possible to defer ant tuberculosis treatment until the acute hepatitis has been resolved. In other cases when it is necessary to treat drug-resistant TB during acute hepatitis, the combination of four non-hepatotoxicity drugs is the safest option.

Seizure disorders

Cycloserine may be given as long as seizure disorder is controlled. Alternative to Cycloserine will be PAS in Kenya. Ensure pre-existing seizure disorder is under control before initiating treatment for drug resistant TB. This may require dose adjustment of the current treatment for the seizure disorder. Examine the drug regimen and modify treatment where feasible for patients who develop seizures during treatment. Such seizures are often due to drug adverse effects.

Psychiatric disorders

Provide psychiatric assessment prior to initiating treatment in patients with existing psychiatric disorders. Provide appropriate psychiatric treatment for patients who develop psychiatric problems while on treatment for drug resistant TB. Consider substituting PAS for Cycloserine in such patients.

DR TB and Substance Dependence

Usually substance abuse is not a contraindication to treatment with anti-TB drugs but appropriate treatment should be offered for the addiction.

Ensure strict DOT for such patients who are at high risk of abandoning treatment
Health care workers should be aware that Cycloserine side effects may be more common in patients dependent on alcohol and other substances.

HIV infection and MDRTB

In Kenya the national co-infection rate is 39% but it varies from one region to another (0% IN NEP and highest in Nyanza North at 50%). The drug management of HIV infected MDRTB patients are challenging especially as regards to pill burden, drug – drug interactions and adverse effects.

The pursuance of recommended TB/HIV interventions as outlined in the NLTP's policy document on TB/HIV collaborative activities is paramount when developing strategies for care and prevention of drug resistant TB in HIV infected persons.

Health care workers need to be aware of the pharmacokinetic interactions between Rifamycins e.g. Rifampicin and protease inhibitors in cases of treatment of mono and poly resistant TB but not MDRTB.

Also health care workers need to be aware that the Fluoroquinolone absorption may be decreased by non-enteric coated didanosine which contains aluminium / magnesium

antacid, therefore the administration of didanosine should be given six hours before or two hours after the Fluoroquinolone

When treating HIV infected patients for MDRTB health care workers should look out for increased drug adverse effects e.g. increased risk of peripheral neuropathy when Stavudine is co-administered with aminoglycosides, increased risk of cutaneous hypersensitivity reactions by all the drugs; increased risk of neuron-psychiatric syndromes with co-administration of Efavirenz and Cycloserine; increased risk of renal impairment by aminoglycosides and adverse gastrointestinal effects by all the drugs.

XIII. Management of Drugs Side Effects

Basics of drug side effects

Patients on second line drugs usually experience many more adverse reactions than those on first-line drugs. It is important for the nurse to check, document and report side effects to the managing clinician at the earliest appropriate time. The following are the basic steps for managing ADRs:

1. Management of ADRs with Standardised Algorithms: For mild ADRs, continue treatment and manage ADRs with ancillary drugs where necessary Many ADRs disappear or diminish with time and patients should be encouraged to tolerate the effects until they subside. Psychosocial support is an important component of management of ADRs.
2. Reduced Dosage of Suspected Drug(s): Some adverse reactions are highly dose dependent. If a patient cannot tolerate the regimen, the dosage of the suspected drug(s) may be reduced until the adverse reactions subside. If reduction of dosage of individual drugs does not result in the disappearance of the ADRs, it may be necessary to reduce the dosages of multiple drugs simultaneously.
3. Removal of Drug(s) from the Regimen: If reduced dosage does not alleviate the ADR it may be necessary to remove a drug from the regimen, or to replace the drug with another drug. This final option should be chosen only as a last resort i.e., in cases of significant organ dysfunction or intractable symptom intolerance

Only the clinical management team should do dose changes or eliminate a specific drug

An urgent clinical meeting should be convened to review any patient with serious adverse effects requiring treatment adjustments

Management of specific adverse reactions

Nausea and vomiting

Suspected agents: PAS, Eto/Pto, Clofazimine, H, E, Z.

Nausea and vomiting are frequent during the first few weeks of therapy and usually cease with supportive therapy. Nausea and vomiting are reversible upon discontinuation of the suspected agent.

1st Phase: Check for signs of dehydration and Hepatitis

- Check signs of dehydration (thirst, dry mouth, sunken eyes, low blood pressure, orthostatic, and weakness) and serum concentration of electrolytes.
- Check out other causes such as hepatitis (jaundice, pruritus, right-sided abdominal pain)
- Adjust administration of medications:
    - -administer ETO or Clofazimine in three separate doses
    - -administer medication associated with nausea at night with short-acting benzodiazepine;
    - -administer PAS one hour after taking other anti-TB medications.

2nd Phase: Administer anti-emetics

- Start with metoclopramide 10 mg by mouth given 30 minutes before dose of anti-TB drugs, to a maximum of 15 mg twice daily.

Note: Avoid metoclopramide if neurological problems develop

3rd Phase

- If metoclopramide is ineffective, start promethazine 25 mg with diphenhydramine 25 mg (or other antihistamine) by mouth 30 minutes prior to anti-TB drugs or prior to meals, up to 3 times daily. This can be increased to promethazine 50 mg (with diphenhydramine 25 mg) 3 times daily to control symptoms. If the patient cannot take drugs orally, give intramuscularly or per rectum.
- Chlorpromazine drops can also be used at a dose of 10-25 mg(available in 25mg/5ml) given 4-6 hourly 30 minutes before DR TB drugs are given

NB: Promethazine is very useful at night for nausea and for sleeping. Side effects of promethazine include sedation, dry mouth, urinary retention, and, rarely, tardive dyskinesia or confusion in the elderly. Diphenhydramine is used to minimize these side effects.

4th Phase

- If persistent vomiting results in dehydration, give 500-1,000 ml of 0.9% NaCl or Ringer's solution intravenously as needed.
- Consider ondansetron 8mg BD for 3 days, then 8 mg OD when necessary.

5th Phase

- If taking ETO, reduce to 750 mg OD
- If taking Clofazimine, reduce to 200 mg OD Note: Cfz can cause the clinical picture of acute abdomen
- If absolutely necessary, stop all anti-TB drugs until symptoms resolve.

Dermatitis

Suspected agents: all are possible - most likely agent is Thioacetazone, especially in HIV infected patients.

1. Rule out other likely causes (i.e., scabies, allergic reaction to non-TB medications).

2. Treatment of localized/mild generalized rash: Give diphenhydramine 25 mg (or other antihistamine) orally up to 3-4 times daily. If itching is severe, apply 1% topical hydrocortisone directly to lesions.
3. Severe/ Bullous/ Exfoliative lesions: **Stop all** medications immediately. A parenteral corticosteroid i.e., IV or IM dexamethasone 2-4 mg 4 times daily may be necessary in severe cases.

After rash has resolved, anti-TB drugs should be added back one at a time 1-2 days apart in gradually increasing doses, in the following order: **H - R - Z – Pto / Eto -Flouroquinolones- Cs - E - PAS – injectable.** If the rash was particularly severe, reintroduce the anti-TB medications starting with one-tenth of the original dose and increase the dose more slowly.

If the rash recurs after resumption of one of these agents, then discontinuation of that agent may be required and another agent should be substituted.

Note: if a rash appears while the patient is on Thioacetazone, stop the drug immediately and administer prednisone at a dose of 1 mg/kg. Do not reintroduce Thioacetazone

Seizures

Suspected agents: Cs, H, and Ofx, Lfx and Mfx

Prior history of seizures is **not** a contraindication to the use of the above agents .Seizures should be controlled in patients with active uncontrolled seizures before starting treatment and the risks and benefits should be discussed with patients.

If patient experiences a seizure for the first time during therapy suspend the Cs for a short period and initiate therapy for seizures, Cycloserine should be reintroduced at a lesser dose but the usual dose should be achieved as soon as possible.

If actively fitting:

1. Place the patient in the lateral decubitus position, remove objects nearby that can cause danger for the patient, protect the tongue with a soft object too large to be swallowed, observe until patient stops seizing,
2. Ensure airway is protected and monitor the patient carefully for signs of respiratory depression
3. Give diazepam 5 mg intravenously or intramuscularly immediately, followed by a loading dose of phenytoin (typically 20 mg/kg intravenously, or orally). Diazepam may be repeated once in 10 minutes if seizures do not cease.If the seizure has already stopped at the time of initial evaluation and the patient is post-ictal, do not give diazepam but give phenytoin loading dose
4. Begin phenytoin maintenance dose of 300 mg/day (3-5 mg/kg/day) once the loading dose has been administered. If seizures recur, phenytoin may be increased to a maximum of 500 mg/day or a second agent (valproic acid, Phenobarbital) may be added
5. Increase pyridoxine to 300 mg/day in all cases.
6. Initiate antiepileptic treatment for the remainder of MDR-TB therapy according to usual prescribed doses.
7. Check electrolytes
8. If seizures recur, refer patient for neurological consultation

Sub-therapeutic levels of anti-seizure drugs can be caused by drug-drug interactions between anti-seizure drugs and anti-TB drugs, especially H and R

Psychosis.

Suspected agents: Cs, Flouroquinolones and H.

Psychotic symptoms refer to a constellation of symptoms that indicates a disintegration of personality or a loss of contact with reality, hallucinations or delusions. The causes of psychotic symptoms in patients with DR TB may be related to socio-economic circumstances and/or underlying psychiatric disease.

Prior history of psychiatric disease is **not** a contraindication to the use of the above agents, though psychiatric side effects are more likely.

Management of Acute psychosis: If the patient is at risk of harming him/herself or others urgent hospitalization is advised.

- Give haloperidol 1 mg orally or intramuscularly, or chlorpromazine 25mg orally or IM.
- If no improvement after 20 minutes, give 2mg and if no improvement after 20 minutes give 4 mg. A benzodiazepine may be given concomitantly provided if there is no evidence of respiratory compromise.
- If good response, start haloperidol 2-4 mg orally once daily and increase pyridoxine to 300 mg/day. Haloperidol may be increased by 2 mg per day to control symptoms, to a maximum dose of 10 mg orally per day. Adjunctive agents that may be useful include clonazepam if haloperidol is not fully effective, and diphenhydramine to control the extra pyramidal side effects of haloperidol
- Risperidone can be used instead of haloperidol. Start with 0.5mg to 5mg bd or tds. The usual dose is 2-10 mg per day. Risperidone is as effective and causes less extra-pyramidal effects than haloperidol.
- Rule out other causes of psychosis, including illicit drugs, alcohol withdrawal.
- Reduce the dose of Cycloserine. It should thereafter be introduced from a low dose of 250mg od for 3 days, if no occurrence of symptoms, this can be increased to 250mg BD for 3 more days and then to 500mg morning and 250mg nocte.
- In the event that the symptoms recur, reduce back to the lower dose. If regimen is compromised consider replacing Cycloserine with PAS. Psychotic symptoms stop once the offending drug is withdrawn.

- **It may be necessary to stop anti-TB therapy temporarily (1-4 weeks) while symptoms are brought under control**
- **Stop Haloperidol immediately the patient develops symptoms of neuroleptic syndrome**
- **Give diphenhydramine 25 mg PO QD If patients develop dystonia, Parkinsonism, or Extra Pyramidal Symptoms.**

Depression

Suspected agents: Cs, flouroquinolones, and H.

Patients receiving anti-TB therapy are subject to a variety of factors (prolonged sickness, separation from family, difficult living conditions, etc.), which should not be underestimated as contributors to depression. Depressive symptoms may fluctuate during therapy. Prior history of depression may increase the risk of developing depression during treatment but is not a contraindication to use of any of the above agents.

Address socio-economic conditions if possible. Promote:

- Supportive counselling by medical and paramedical (i.e., health educators, social workers) staff.
- Intensive psychological therapy with counselling to patient and family.
- Emotional support from the family and health promoter.
- Group therapy or informal support groups

Always give pyridoxine 50mg per 250mg of Cs.

If necessary, initiate antidepressant medication (i.e., amitriptyline or fluoxetine) according to usual prescribed doses. Consider lowering the dose or discontinuing a suspected anti-TB agent provided this does not compromise the effectiveness of the regimen.

Note*: when the regimen contains H: avoid fluoxetine and clomipramine; treat with amitriptyline*.

Peripheral neuropathy

Suspected agents: S, Km, Cm, H, FQ, Cs, and E (rarely PTO / Eto).

Patients with co-morbid disease such as diabetes or alcoholism are more likely to develop neuropathy, but such conditions are not a contraindication to use of the above agents.

Management:

- Increase pyridoxine to 200mg/day
- If the patient is on Km change the parenteral agent to Cm.
- Advise on physical therapy focusing on the affected region
- If the above measures are ineffective, begin nortriptyline or amitriptyline (tricyclic antidepressant-TCA) 25 mg orally at bedtime, increasing the dose by 25 mg each week to a maximum of 100-150 mg until symptoms are controlled.

  Peripheral neuropathy can have several forms; TCA typically work with chronic constant pain, can be supplemented by NSAIDS; 'shooting' pain responds well to carbamazepine and valproate
- If no improvement, start carbamazepine 200mg BID and increase to 600mg BID. Consider use of phenytoin.
- If not controlled, refer for a neurological consultation and decrease dose of responsible medication: Cs to 750mg and Km/Am 750mg if Cm not available. Resume normal dose once pain controlled.

  Neuropathy is generally not reversible upon discontinuation of anti-TB therapy, but only a small minority of patients requires long-term treatment to control symptoms.

Drug-induced hepatitis

Suspected agents: Z, H, R, PTO / ETO, and PAS.

As part of regular monthly screening, examine patient for signs and symptoms of hepatitis (i.e., anorexia, nausea, vomiting, abdominal pain, jaundice, dark urine, pale stools) . Incase of any signs of hepatitis:-

- Do hepatitis B surface antigen and Liver function tests
- If liver enzymes elevated but less than 5 times normal, continue anti-TB therapy but follow liver function tests each week.
- If liver enzymes greater than 5 times normal, stop all anti-TB medications and repeat liver function tests weekly. If liver enzymes continue to worsen, then progressive drug-induced hepatitis or an unrelated cause must be suspected.
- If liver enzymes plateau or revert to normal and symptoms resolve, one may restart anti-TB drugs one at a time over a period of one week beginning with the agents least likely to be hepatotoxic: **Injectable – Cycloserine - Flouroquinolone–Eto/ Pto -Z. Check LFTs at the end of each week.** The offending agent can generally be identified in this manner and discontinued or replaced.
- If symptoms fail to resolve, consider lowering the dose of the suspected agent provided this does not significantly compromise the effectiveness of the treatment regimen.

Hypothyroidism

Suspected agents: PAS, PTO / ETO (particularly when given in combination).
Signs and Symptoms include fatigue, weakness, cold intolerance, decreased appetite, and constipation, loss of energy, depression, inability to concentrate,enlarged thyroid, dry skin, coarse hair, and weight gain. If present:

- Check TSH level .If TSH level is greater than 10, then symptomatic hypothyroidism is likely and therapy should be given.
- Levothyroxine therapy should be initiated at a dose of 50µg daily (or 25µ g daily for patients older than 65 years), increasing the dose by 25 µg and checking a TSH level every 4 weeks until a normal level is attained.
- Thereafter TSH should be checked every month until the patient's course of anti-TB therapy has been completed.
- If symptoms do not improve, lower PTO dose by 250 mg or decrease PAS to 4 gm twice daily. Discontinue the drug(s) if above measures are ineffective and equally effective agents can be substituted.

Note: *Hypothyroidism is reversible upon discontinuation of PAS and/or Eto/Pto, i.e., the TSH level normalizes after 2-3 months.*

Do not give levothyroxine at same time as antacids or phenytoin, as these impair GI absorption.

Renal failure

Suspected agents: aminoglycosides, Cm.

Renal impairment may be permanent following treatment with the above agents.

Co-morbid conditions such as diabetes or chronic renal failure are not a contraindication to treatment with the above agents, though greater caution must be exercised in such circumstances.

Acute renal failure presents with : Diminished urine production (< 0.5 ml/kg/hour or < 30 ml/hour), oedema/anasarca, malaise, nausea orincreased difficulty breathing

Management:

- Suspend the nephrotoxic agent.
- Rule out other causes of renal failure (e.g. diabetes, dehydration, congestive heart failure, urinary obstruction, urinary tract infection, prostatic hypertrophy)
- Monitor serum creatinine and electrolytes closely until renal function stabilizes or improves and then resume the parenteral agent
- Switch to Cm if an aminoglycoside was being used previously.
- Reduce the frequency of the injectable. Give the injectable, Cycloserine and Pyrazinamide 3 times a week and monitor creatinine and electrolytes levels monthly.

Electrolyte loss

Suspected agents: Cm, aminoglycosides, PAS, (rarely PTO / ETO)

Hypokalaemia (defined as serum potassium less than 3.5meq/L) and hypomagnesaemia (defined as serum magnesium less than 1.5 meq/L) are not uncommon in patients receiving MDR TB therapy and are caused by the following:

- Direct renal tubular effect of aminoglycosides and Capreomycin.
- Vomiting and diarrhoea.

Patients are often asymptomatic but may present with fatigue, myalgia, cramps, paraesthesia, lower extremity weakness, behaviour or mood changes, somnolence, and confusion. Severe disturbances can lead to tetany, paralysis, and life-threatening cardiac arrhythmias.

All patients with significant GI losses and in all patients receiving parenteral therapy should have electrolyte levels monitored.

Once hypomagnesaemia or hypokalaemia is diagnosed, the following actions should be taken:

- Underlying causes such as vomiting and diarrhoea should be treated.
- Arrhythmogenic medications (such as digoxin, tricyclic antidepressants) should be discontinued if possible.
- An electrocardiogram should be performed in patients with significant electrolyte disturbances; if the QT segment is prolonged, any drugs contributing to QT prolongation – including certain flouroquinolones, haloperidol, fluconazole, and cisapride – should be held.

Treatment of hypokalaemia and hypomagnesaemia:

1. Do UECs. Confirm renal function prior to instituting repletion. Patients with renal failure will require smaller doses.
2. Supplement potassium and Magnesium. When possible, potassium depletion should be corrected orally by increased dietary uptake or supplementation with potassium salts. Intravenous treatment is required for patients with gastrointestinal disorders or severe potassium deficiency
3. When giving Oral KCL, the tablets may be diluted in water or taken as pills. The dose may be split and given two or three times per day. Supplement diet with banana, orange/tomato/avocado/grapefruit juice.
4. When giving IV Supplementation the dose should **NOT** exceed 20 meq/hr. of KCl. Normal preparation is 40 meq in 1 litre of NaCl 0.9%; maximum preparation is 60 meq/L.
5. Serum magnesium levels are not always reflective of total body magnesium content, empiric magnesium replacement is often needed in hypokalaemia even if the serum magnesium levels are within normal range
6. Potassium-sparing diuretics (spironolactone, triamterene, or amiloride) may be used as adjuvant therapy in severe renal potassium losses to decrease renal loss of K and Mg: Amiloride 5–10 mg per day or Spironolactone 25–50 mg per day. **Caution**:Hyperkalaemia may result when potassium-sparing diuretics are given in conjunction with potassium supplements

- **Capreomycin is more often associated with electrolyte loss than other injectable agents. Consider changing CM to AMK or KM if the strain is susceptible.**
- **If electrolyte abnormalities do not correct once the injectable is suspended suspect another cause.**
- **Hypomagnesaemia often causes hypokalaemia and hypocalcaemia. Hypokalaemia and hypocalcaemia will be refractory to treatment unless hypomagnesaemia is also treated**
- **The magnitude of total body depletion of potassium (K^+) and magnesium (Mg^{++}) may be far lower than that which is reflected in serum levels.**
- **Electrolyte Replacement may be needed during the whole course of the use of the aminoglycoside or capreomycin.**

Treatment of Hypocalcaemia

- Determine if true hypocalcaemia is present by **adjusting** total serum calcium levels for low albumin .This is done by adding 0.8 mg/dL for every 1 g/dL decrease of serum albumin below 4 g/dL (ionized levels of calcium do not need to be adjusted).
- Treat symptomatic hypocalcaemia as an **emergency** .Administer 2 grams of calcium gluconate (180 mg elemental calcium or 20 ml 10% calcium gluconate) IV over 10 minutes, followed by infusion of 6 grams calcium gluconate in 500 ml D5W over 4–6 hrs. The IV infusion should be tapered.

- The initial oral dose during the transition from IV to oral therapy is 1–2 g elemental calcium three times a day.For long-term therapy the typical dose is 0.5–1.0 g PO TID.

Frequency and replacement table for potassium

Table 3.47: Frequency and replacement table for potassium

Potassium level meq/L	Dose KCl in meq	Frequency of monitoring (sooner if patient has vomiting / diarrhoeal)
Above 3.7	None	Monthly
3.4-3.6	20-40	
3.0-3.3	60	
2.7-2.9	80	
2.4-2.6	80-120	
2.0-2.3	60 IV and 80 P.O every 6-24 hrs.	Hourly after infusion until serum K^+ is > 2.8 meq/L
< 2	60 IV and 100 P.O every 6 hours	Hourly after infusion until serum K^+ is > 2.8 meq/L. Consider withholding injectable until > 2.4

Oral Potassium replacement

Table 3.48: Oral Potassium replacement

Serum K^+(mmol/l)	Dose of Slow-K(mg)
3.3 - 3.5	1200mg tds (6tabs = 48mEq,per day)
2.9 – 3.2	1800mg tds (9tabs = 72mEq, per day)
2.5 – 2.8	2400mg tds (12tabs = 96mEq, per day)
≤ 2.4	3000mg tds (15tabs = 120mEq, per day)

Frequency and replacement table for calcium

Table 3.49: Frequency and replacement table for calcium

Calcium level (Total calcium adjusted for low albumin)	Dose of calcium	Frequency of Monitoring
>8.5 mg/dL	None	
7.5-8.4	500mg TID	Monthly
7.0-7.4	100mg TID	1-2 weeks
<7.0	Consider IV and tapper to 1000mg TID	1-4 days

Frequency and replacement table for magnesium (Available as Magnesium gluconate or Magnesium oxide)

Table 3.50: Frequency and replacement table for magnesium

Magnesium level meq/L	Total daily dose mg	Frequency of monitoring
>1.5	None	Monthly
1.1-1.4	1000-1200	Monthly
0.8-1.0	2000 (consider IM)	1-2 weeks1-6 days
<0.8	3000-6000MG (Give IV or IM)	

NOTE: This table assumes that a 400 mg tablet will contain 240 mg elemental magnesium. Check the preparations you are using and if they have less elemental magnesium, you may have to increase the tablet dosage

Guidance on IV Supplementation of Magnesium

- Maximum concentration: 5 g or 40 meq $MgSO_4$ in 1 litre of NaCl 0.9% or dextrose 5%
- Do NOT exceed 150 mg per minute.
- If not emergency:
    - 2 g in 100 ml administered over 1–2 hours
    - 4 g in 250 ml administered over 2–4 hours

Guidance on Intramuscular Supplementation of Magnesium

- 1 g (or up to 250 mg/kg) of $MgSO_4$ without dilution IM every 6 hours.
- No advantage over IV magnesium.
- Indicated if supplementation cannot be received PO or IV.

Common Side Effects, the Likely Agents Responsible, and Suggested Management Strategies

Table 3.51: Common Side Effects, the Likely Agents Responsible, and Suggested Management Strategies

Side affect	Suspected agent(s)	Suggested management strategy	Comments
Gastritis (Dyspepsia, belching, hyperacidity and epigastric pain)	PAS Ethionamide H E Z CFZ	-Take medication after meals -Start with aluminium hydroxide 2-4 tablets orally up to 4 times daily, at least 2 hours before or after anti-TB medications. -If symptoms persist: Treat with omeprazole 20 mg once a day by mouth. -If this treatment is not successful, medically re-evaluate while considering other aetiologies.	-Antacids should be administered at least 2 hours before or after taking anti-TB drugs so as not to interfere with the absorption of anti-TB drugs -Monitor electrolytes especially potassium and replace

Nausea and vomiting	PAS Pto H E Z CFZ	- Assess for dehydration. Initiate rehydration if indicated. - Initiate anti-emetic therapy.(Refer to notes on stages of management) - Lower dose of suspected agent, if this can be done without compromising regimen.	- Nausea and vomiting are common in the early weeks of therapy and usually **abate** with time on treatment and supportive therapy. - Electrolytes should be monitored if vomiting is severe. - Reversible upon discontinuation of suspected agent. - Clofazimine rarely causes severe abdominal distress and acute abdomen .If this occurs,Clofazimine should be suspended.
Diarrhoea	PAS, PTO / ETO.	**-Mild diarrhoea**: Give loperamide 4 mg by mouth initially followed by 2 mg after each loose stool to a maximum of 10 mg per 24 hours. Encourage fluid intake. **-Severe**: Admit and give IV fluid. Rule out acute other causes	- Since many patients use the term diarrhoea to describe bowel movements that are more frequent or loose than normal, it is important to note whether the stool is truly watery and more than three or four times a day. -If bloody stools, severe abdominal pain, or fever greater than 38.5 ˚C, consider other causes such as acute bacterial enteritis, or pseudo-membranous colitis related to flouroquinolones.
Seizures	Cs H FQ	-Suspend suspected agent pending resolution of seizures -Increase pyridoxine to a maximum daily dose (200 mg per day) -Initiate anticonvulsant therapy. **Refer to notes for detailed management** -Reinitiate suspected agent at lower dose, if essential to the regimen	-Anticonvulsant is generally continued until MDR TB treatment is completed or suspected agent discontinued

Peripheral Neuropathy	CS H FQ KM AMK CM E Ethio	-Increasing pyridoxine to a maximum daily dose (**200 mg per day**). **-Change** parenteral to CM if the patient has documented susceptibility to CM. -Initiate tricyclic antidepressants such as amitriptyline. NSAIDS or acetaminophen may help alleviate symptoms. -Lower dose of suspected agent, if this can be done without compromising regimen.	-Patients with co-morbid disease (e.g., diabetes, HIV, alcoholism) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here. -Neuropathy may be irreversible; however, some patients may experience improvement once offending agents are stopped
Arthralgias	Z FQ	-Initiate therapy with non-steroidal anti-inflammatory drugs. -Initiate exercise regimen. -Lower dose of suspected agent, if this can be done without compromising regimen.	-Symptoms of arthralgia generally diminish over time, even without intervention. -Uric acid levels may be elevated in patients on pyrazinamide. Allopurinol **appears not to** remediate uric acid levels.
Hearing loss	S KM AMK CM	-Document hearing loss and compare to baseline Audiometry -Change parenteral to CM if patient has documented susceptibility to CM	-Patients with prior exposure to amino glycosides may have a baseline hearing loss. Obtain Audiometry at the initiation of MDR TB therapy. -Hearing loss is **generally not** reversible.
Optic neuritis **(**Loss of red-green Colour distinction is usually the first sign)	E	-Stop E permanently -Refer patient to an ophthalmologist	-Usually reverses with cessation of E. -Rare case reports of optic neuritis have been attributed to streptomycin

Psychotic symptoms	Cs, H, FQ, Ethio	-Usually caused by Cs. Withhold suspected agents until symptoms are brought under control. -Initiate anti-psychotic drugs e.g. Haloperidol -Start Cycloserine at 250mg per day, observe for 5 days, If stable increase to 250mg BD for 5 days. Increase the dose again to 750mg per day. If the patient cannot tolerate, reduce to where the patient can tolerate. **NB. Cycloserine is given in divided doses.** - In case of severe psychosis, replace with PAS	-Some patients will need to continue anti-psychotic treatment throughout MDR TB therapy. -Prior history of psychiatric disease is **not a contraindication to the use of agents** listed here but may increase the likelihood of developing of psychotic symptoms. -Psychotic symptoms **are generally reversible** upon completion of MDR TB treatment or cessation of the offending agent
Depression	Socioeconomic Circumstances, Chronic disease, CS, FQ H Ethio	-Improve socioeconomic conditions. -Group or individual counselling. -Initiate antidepressant drugs. -Lower dose of suspected agent, if this can be done without compromising the regimen. -Withhold the suspected agent for a short period as symptoms reside (one to four weeks) and reinitiate therapy	-Socioeconomic conditions and chronic illness should not be underestimated as contributing factors to depression. -Depressive symptoms may fluctuate during therapy and may improve as illness is successfully treated. -History of prior depression is not a contraindication to the use of the agents listed here; however, these patients may be at increased risk for developing depression during MDR TB treatment
Hypo-thyroidism	PAS Pto/Ethio Especially when given in combination	-Initiate Thyroxin therapy(Refer to notes) -Thyroxin should be given for till one month after completion of treatment -Follow TSH and adjust thyroxin periodically	**-Completely reversible** upon discontinuation of PAS or Ethio. -Generally, no need to suspend suspected agents

Hepatitis	Z /R/H/E Ethio /PAS FQ	-Rule out other potential causes of hepatitis. - If the LFT results shows a **>5 times** than the reference range Stop all therapy pending resolution of hepatitis.	-Re-introduce remaining drugs, one at a time with the **LEAST** suspected hepatotoxic agents first, while monitoring liver function(Refer to notes)
Renal failure	S KM AMK CM	-Substitite amino glycoside for CM -Consider using intermittent dosing while monitoring the Creatinine clearance -Adjust all TB medications according to the Creatinine clearance	-History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure. -Renal impairment may be permanent
Electrolyte disturbance (Hypomagne-saemia & Hypokalemia	CM KM AMK S	-Check potassium.If low, also check magnesium and calcium - **Admit** patient if Severe Hypokalemia is present -Replace electrolytes as needed(Refer to notes)	-Amiloride 5-10 mg QD or spironolactone 25 mg QD may decrease **potassium** and **magnesium** wasting and is useful in refractory cases. -Electrolyte disturbances most commonly observed with Capreomycin

Adverse effects of MDR-TB/ART co-treatment

Table 3.52: Adverse effects of MDR-TB/ART co-treatment

Signs or symptoms	Response
Abdominal pain	May be caused by several drugs. The patient should take drugs with food (except for ddI or IDV). Treat symptomatically
Nausea, vomiting	May be caused by many drugs. If due to ARV, they will often improve in a few weeks. If due to Ethionamide or PAS, nausea or vomiting may be chronic. Check for other causes of vomiting
Diarrhoea	If due to ART, the diarrhoea will improve in a few weeks. If it is due to PAS, it may be chronic If the patient is dehydrated, re-hydrate with ORS or an IV line. Examine, and treat for other possible causes of diarrhoea
Fatigue	Consider hypokalaemia or renal failure as a cause. Check creatinine, potassium Consider anaemia as a cause and check haemoglobin. Consider hypothyroidism due to Ethionamide and PAS and check TSH

Depression, anxiety, nightmares,	These may be due to EFZ or Cycloserine/Terizidone. If they are due to EFZ, symptoms will usually last less than three weeks. Mild depression can be managed with amitriptyline at night. Call for advice or refer if the patient has severe depression or is suicidal or psychotic. Serious symptoms may improve with a decreased dose of Cycloserine/ Terizidone
Itching of skin, skin rash	If these symptoms are mild, give an antihistamine and monitor closely. If the patient has recently started NVP and is not responding to antihistamine, consider changing NVP for EFZ If the itching is generalized, or there is skin peeling, mucosal involvement, or other symptoms (fever, jaundice, etc.) stop all drugs (including CTX). This is very serious. Drugs will need to be reintroduced carefully when the rash has been resolved. Call for advice.
Jaundice (yellow skin or eyes)	Check the patient's liver function tests (AST, ALT, and bilirubin) and stop all drugs. The jaundice may be due to EFZ, NVP, pyrazinamide or Ethionamide or other drugs. Call for advice on how to restart drugs
Pallor: anaemia	Measure the patient's haemoglobin. Anaemia may be a sign of an undiagnosed OI. AZT may cause anaemia, often in the first four to six weeks. If the patient has severe pallor or very low haemoglobin (<8 g/ dl; <7 g/dl in a pregnant woman), stop AZT/substitute d4T. Refer/consult
Neuropathy (burning sensation in feet)	This may be due to ddI, d4T, Cycloserine/Terizidone, isoniazid, injectable or other drugs. Stop Stavudine and replace with Zidovudine. If patient shows no improvement, start amitriptyline or carbamazepine and call for advice
Muscle cramps, muscle spasms	The patient may have electrolyte wasting. Check potassium immediately; replace low potassium with bananas or potassium supplements
Headache	Give patient Paracetamol. Assess for meningitis. If patient is on AZT or EFZ, reassure him/her that this is common and usually self-limited. If headaches are chronic, they may be due to Cycloserine
Renal failure (swelling, decreased urine, hypertension)	Check creatinine. Stop injectable and call for advice
Hypothyroidism (fatigue, slowing)	Due to Ethionamide and PAS. Do not stop any Medications. Give thyroxin 50-100 mcg/day and recheck. The thyroid will return to normal once MDR-TB treatment is over
Blue/black nails	Reassure. It is normal with AZT
Gradual hearing loss (confirm that this is not due to ear wax)	May be due to injectable. Refer or consult
Dizziness, lack of balance	May be due to injectable. Refer or consult
Changes in fat distribution	Due to d4T or ddI. Discuss this carefully with your patient—can she/he accept it?

Suggested Further Reading

1. Guidelines for the programmatic management of drug-resistant tuberculosis: World Health Organization, (2006 WHO/CDS/TB/2006.361)
2. Treatment of tuberculosis: Guidelines for national programs, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003)
3. Laboratory services in tuberculosis control. Parts I, II, and III. Geneva, World Health Organization, 1998 (WHO/TB/(98.258)
4. Laserson KF et al. Speaking the same language: treatment outcome definition for multi drug-resistant tuberculosis. International journal of Tuberculosis and lung disease, 2005, 9(6): 640-645
5. Scaaf HS et al: Evaluation of young children in contact with adults Multidrug-resistance pulmonary tuberculosis: a 30-month follow-up. Paediatrics, 2002,109 (5): 765-571.
6. Texeira L et al. Infection and disease among household contacts of patients with MDR-TB. International journal of tuberculosis and Lung Disease, 2001,5 (4): 321-328
7. Kritski Al et al. Transmission of tuberculosis to close contacts of patients with Multidrug resistant TB. American journal of Respiratory and critical Care Medicine, 1996,153 (1): 331-335.
8. Zigol M et al. journal of infectious diseases. 2006; 194:479-85.

CHAPTER 4

LEPROSY

Background and Introduction

Definition of Leprosy

Leprosy is a chronic infectious disease caused by *M*ycobacterium leprae. It mainly affects the skin, peripheral nerves and mucous membrane. The incubation period from infection to clinical manifestations is variable, it is shorter for Paucibacillary (PB) disease (in the order of 2–5 years) than for Multi-bacillary (MB), in the order of 5–10 years and sometimes much longer.

Source of Infection

Untreated Multi-bacillary leprosy patients discharging bacilli are the main source of infection

Epidemiology and History of Leprosy

Leprosy is one of the oldest documented diseases in the world. It is mentioned in the Bible, Koran and other religious book. However, the description in these books may include other dermatological conditions with similar manifestations.

Globally over 200,000 leprosy cases are reported in the year 2013 with majority of leprosy patients being found in South East Asia, Americas and Africa. Kenya is in the post elimination phase, 133 cases were notified in the year 2014, majority (90%) of the cases were Multibacilary (infectious type). Leprosy Endemic counties include: Kilifi, Kwale, Malindi, Kisumu, Siaya and Busia. Despite the apparent low number of cases reported annually in Kenya, 11% of the cases notified in 2014 were below 15 years. This suggests stable active transmission of leprosy in the community.

Population Affected

Leprosy affects persons in all age groups and both sexes. The age group mainly affected is between 15 and 45 years. Factors related to poverty increase the risk of developing the disease.

Pathophysiology

Bacilli enter the body usually through respiratory system. It has low pathogenicity, only a small proportion of infected people develop signs of the disease. Though infected, majority of the population do not develop the disease. After entering the body, bacilli migrate towards the neural tissue and enter the Schwann cells. Bacteria can also be found in, macrophages, muscle cells and endothelial cells of blood vessels.

After entering the Schwann cells /macrophage; fate of the bacterium depends on the resistance of the infected individual towards the infecting organism. Bacilli start multiplying slowly (about 12-14 days for one bacterium to divide into two) within the cells, get liberated from the destroyed cells and enter other unaffected cells. Till this stage person remains free from signs and symptoms of leprosy.

As the bacilli multiply, bacterial load increases in the body and infection is recognized by the immunological system. Lymphocytes and histiocytes (macrophages) invade the infected tissue. The bacteria do not produce any toxin, but induces inflammatory reaction that leads injury of the nerve, demyelination, and consequent disability. Damage to one or more of the three components of the nerve with different sequelae:

- Sensory fibres: loss of sensation
- Motor fibres: weakness or paralysis in innervated muscles
- Autonomic fibres: dryness and hypo-pigmentation of the innervated skin

At this stage clinical manifestation may appear as involvement of nerves with impairment of sensation &/ or skin patch. If it is not diagnosed and treated in the early stages, further progress of the diseases is determined by the strength of the patient's immune response.

Mode of Transmission and Risk Factors

Leprosy is a droplet infection transmitted from a source patient through, coughing and sneezing. Infectiousness of leprosy patients is related to the size of the bacillary population in the body.

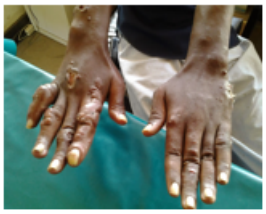
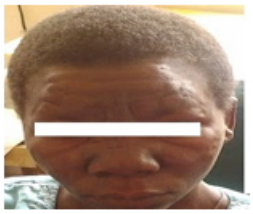
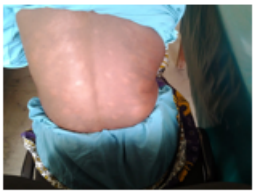
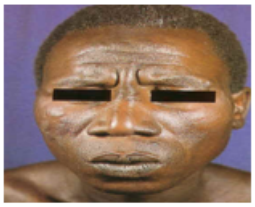
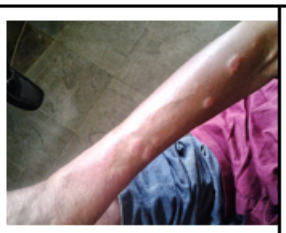
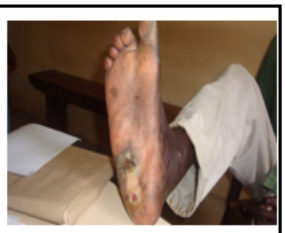
Infection follows prolonged contact with an infectious leprosy patient. Closeness of contact is related to the dose of infection, which in turn is related to the occurrence of disease. Contacts of MB cases are 5-10 Times, and contacts of PB cases 2-3 times, more likely to contract clinical leprosy than individuals in endemic communities with no known contact with recognized cases.

Clinical Presentation of Disease

Signs and symptoms include:

- Burning sensation in the skin
- Areas of anesthesia in the skin with no skin patches (Neural leprosy)
- Pale patches on the skin with loss of sensation to cotton wool touch
- Numbness and tingling sensation in the feet and/or hands
  Weakness of the eyelids, hands or feet

- Tender nerves
- Painless swelling or lumps, especially in the face and ear lobes
- Painless wounds and unnoticed injuries and burns on the hands feet and eyes
- Joint pains
- Swollen nerves

			
Leprosy patches	Leprosy nodules	Nodules on earlobes	Thickened (leonine)
			
Leprosy patches	Leprosy patches on	ENL reaction	Painless wounds

WHO Cardinal signs

In an endemic country or area, an individual should be regarded as having leprosy if he or she shows ONE of the following cardinal signs:

- Skin lesion consistent with leprosy and with definite sensory loss, with or without thickened nerves.
- positive skin smears

Suspect case of leprosy

- Nodules on the skin with no other evidence
- One or more suggestive skin patches with normal sensation
- Extensive loss of sensation in the hands or feet with no other evidence of leprosy
- One or more grossly enlarged peripheral nerve trunks with no sensory loss or skin lesion
- Painful nerves with no other evidence of leprosy

Painless ulcers on hands and/or feet with no other evidence of leprosy

Diagnosis of Leprosy

Diagnosis of leprosy requires a high index of suspicion. A proper clinical history and physical examination are critical in making a diagnosis of leprosy.

Clinical Diagnosis

Clinical entails taking a detailed history and proper physical examination in a room with good lighting.

Clinical History

History of presenting illness.
Ask for the duration and progress of symptoms, history of leprosy in the family or prolonged contact with a leprosy patient and treatment history.

Systemic Review

A thorough review of the systems should be done however the following systems should specifically be reviewed.

1. Skin

Ask the patient about skin discoloration and duration of its presence, Presence and duration of nodules and itchiness in the skin.

2. Nervous system

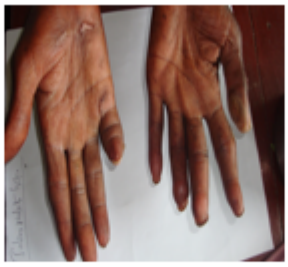
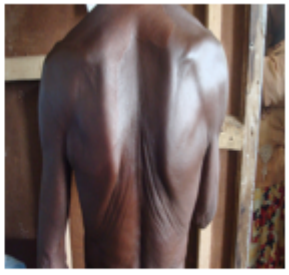
Specifically ask about weakness of muscles of hands, feet and eyes as well as loss of sensation in these parts.

3. Musculoskeletal

Ask for history of unnoticed injuries in the hands feet and eyes

Physical examination

Examine the patient in good lighting focusing mainly focus on the skin and the nervous system. Specifically look for hypo pigmented skin lesions, weakness of muscles and ulcers

		
Examining for sensation on a patch	Examination for scars, wounds, and wasting of muscles	Examine the whole body for any patches

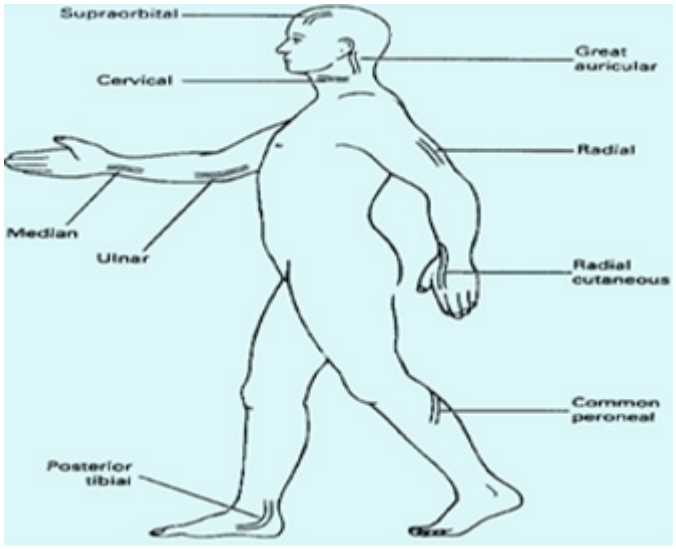
Skin

Look for hypo pigmented skin patches with loss of sensation use cotton wool to examine for light touch). Examine for nodules. Look for dryness cracks and hair loss on the patches and the eye brows lashes. Examine for muscle wasting.

Nervous

Systematically examine the peripheral nerves for nerve enlargement tenderness and loss of function (autonomic, sensory and motor)
The following peripheral nerves are usually affected with different consequences and must be examined.

Sites where peripheral nerves can be palpated are shown below



Facial Nerve

Facial nerve damage leads to facial palsy (weakness in the muscles of the face).
When the orbital branch is affected the patient will present with difficulty in closing the eyes (lagophthalmos (rabbit-like eyes).

Trigerminal Nerve

Damage to the trigeminal nerve leads to loss of the blink reflex resulting dryness and exposure keratitis. While examining the patient, observe for blinking.
The damage causes loss of sensation of the cornea leading to frequent injuries of the cornea by foreign objects. This may result to infection, healing with fibrosis, opacity formation and blindness. The eyes should always be examined for injuries.

Great Auricular Nerve

The nerve usually runs across the neck. In leprosy the nerve enlarges and a firm rod-like structure may be seen and felt under the skin. There is usually no obvious loss of function. The enlargement of this nerverve is almost confirmatory of the presence of leprosy.

Radial Nerve (high radial)

When damaged it leads to a wrist drop.

Ulna nerve

The nerve runs in the olecranon groove in the medial aspect of the elbow joint. When damaged it leads to dryness in the hypothena eminence, the fifth finger and the medial aspect of the forth (ring finger), it also leads to loss of sensation in the same area. There is also wasting of the hypothena eminence and clawing of the

forth and the fifth fingers. The ulna nerve also supplies the intrinsic muscles of the hand. Therefore damage results in ridging of the hand due to muscle wasting.

Median Nerve

This nerve runs deep under the flexor retinaculum sheath in the wrist and therefore difficult to palpate. When inflamed it is possible to elicit tenderness when one presses over the anterior aspect of the wrist joint. Damage of the median nerve manifects as dryness, cracking and loss of sensation in the thenar eminence, the thumb, the 2nd, 3rd and the lateral aspect of the 4th finger. There is also wasting of the thenar eminence and ridging of the dorsum of hand as seen in ulna nerve damage. Wasting of the thenar eminence leads to loss abduction resulting ape thumb and clawing of the thumb 2nd and 3rd fingers.

Radial Cutaneous Nerve

There is no obvious loss of function but the nerve is useful in confirming the diagnosis of leprosy when enlarged. This nerve can be palpated on the lateral aspect of the distal end of the radius proximal to the wrist.

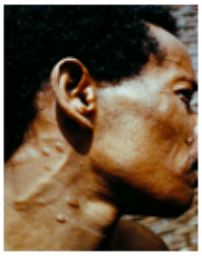
Common Peroneal Nerve (lateral popliteal)

The common peroneal nerve can be felt just below the head of fibular below the knee arising from the popliteal fossa. This nerve is responsible for dorsiflexion and evarsion of the foot. When damaged it leads to plantar flexion and invarsion of the foot (foot drop). Observe the patients for evidence of foot drop while walking.

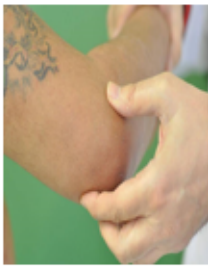
Posterior Tibia Nerve

Posterior tibia nerve is palpated below the medial malleolus. It is responsible for autonomic sensory and motor functions of the foot. Damage leads to dryness and cracks in the sole of the foot, loss of sensation wasting of the sole foot pad leading to the loss of the foot arch (flat foot) resulting in plantar ulcers (mechanical ulcers).

Palpating for supra orbital nerve



Enlarged great auricular nerve



Palpation of left - ulna nerve

Laboratory diagnosis of leprosy

Where available, laboratory tests may be used to confirm the diagnosis of leprosy especially among Multibacilarycases. These include:

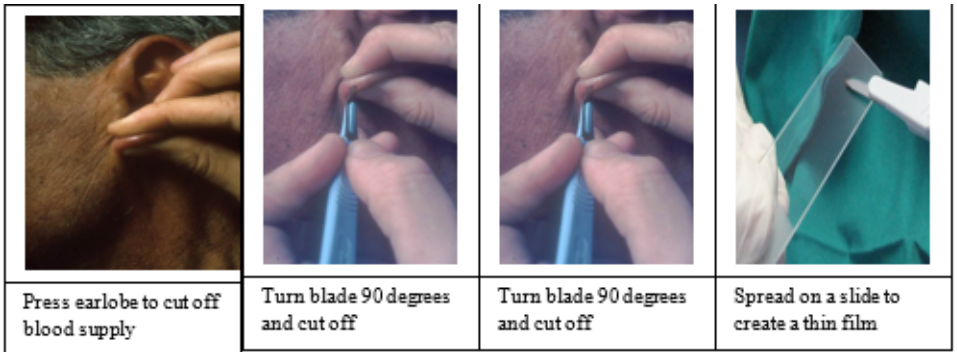
- Bacteriological
- Histological
- Molecular methods

Bacteriological

Slit skin smears

Smears can be taken from any area of the body that manifest leprosy like a patch a nodule area of anesthesia or infiltration. In practice smears are commonly taken from ear lobes, one elbow, and a contra lateral knee.

Slit skin smear Procedure is as follows:
NB- use gloves and ensure aseptic procedure.



Nasal swabs

A special forceps is inserted into the nose to open it up and cotton swab used to scrap materials from the nasal wall. The smears are then prepared on a microscope slide for staining. This is not recommended due to the presence of normal mycobacterial flora in the nose.

Histology

Skin or nerve biopsies can be taken for histological examination using various histological techniques like, ZN, FITES, etc.

Molecular techniques

Molecular techniques can be used to detect genetic materials of M.leprae for example PCR.

Differential Diagnosis

Leprosy is primarily a disease of the nerves, particularly the cooler, peripheral nerves. It secondarily affects the skin.

Differential diagnosis related to the skin

Some of the skin manifestations that may be confused with leprosy include hypo pigmented non-raised (macules) and raised lesion (plaques).

Non-raised Hypo Pigmented Lessions (Macules)

Birth Marks (Nevus Achromicus)

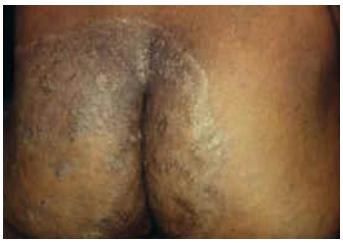
Well defined white patches that are persistent from birth and increase in size with growth of the body. Hairs on the patches are also depigmented.

Vitiligo or Leukoderma

While in true leprosy there is only a partial loss of pigment of the skin, in this condition, there is a total loss of pigment (skin is white), although in the early stages of leukoderma, the patches are hypopigmented and can be confused with indeterminate leprosy. There is no sensory deficit in the patches.

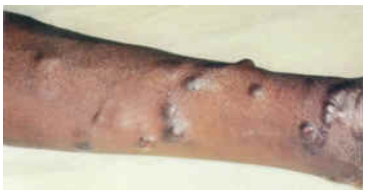
Tinea Versicolor

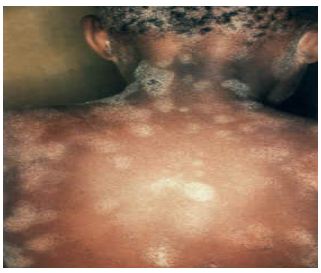
The neck and trunk are the prime sites. Generally, the lesions are multiple and have no loss of sensation. Fungi can be seen under the microscope.



Pityriasis Rosea

Lessons manifest as small oval patches on the trunk. The scaly lesions can be confused with leprosy but there is no loss of sensation.





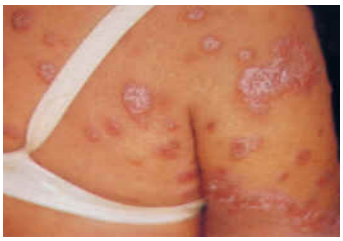
Raised Hypopigmented Lesions: (Papules / Plaques/ Nodules)

Seborrhoeic Dermatitis

The lesions are yellow colored and show coarse parakeratotic scaly lesions which are common on the chest and back and they may coalesce into larger polycyclic patches healing in the center. Itching is usually mild.

Tinea Corporis

These lesions, generally known as "Ringworm", usually present in the groin and waist area. Unlike a leprosy patch, they are always itchy and fungal elements can be seen under the microscope. There is no loss of sensation.



Psoriasis

Silvery white patches of psoriasis have no sensory loss.

Kaposi's sarcoma

Kaposi's sarcoma lesions are often found on the foot or leg. The lesions are shiny, violaceous and nodular. Sensation is preserved.

Multiple Neurofibromatosis

Characterized by growth of non-cancerous tumors in the nervous system. The commonest tumors are acoustic neuromas. The most Common signs include hearing loss, ringing in the ears (tinnitus) and problems with balancing. Some people may develop cataract.

Diabetic ulcers can often be confused with ulcers following neglected leprosy

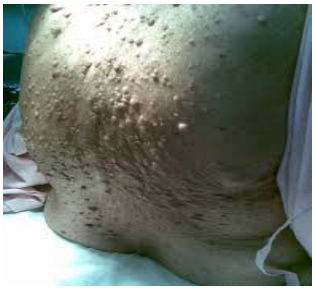
Differential diagnoses relating to nerves

Vitamin B deficiency

This may be seen in undernourished children and alcoholics. Loss of sensation in the lower limbs can sometimes be experienced by those suffering from Vitamin B12, resulting in lesions in the posterior column of the spinal cord.

Toxic Neuritis

Patients working in paint factories or other heavy metal industries dealing with lead, arsenic etc. may develop a leprosy-like anesthesia and paralysis. Careful recording of case histories is essential.



Syphilitic Neuritis

This is another disease affecting the posterior column of the spinal cord, resulting in lesions that lead to sensory loss. A careful case history needs to be taken a V.D.R.L. test made.

Traumatic Neuritis

A careful recording of case history may reveal physical injury to the nerve, perhaps through an accident.

Diabetes Mellitus

Many patients with ulcerated feet have been wrongly diagnosed as having leprosy because peripheral neuritis in diabetes can result in loss of sensation, particularly in the lower extremities which often produces trophic or plantar ulcers. A careful physical examination will reveal glicosuria and hyperglycemia.

Bell's Palsy

This condition results from Facial Nerve involvement causing facial paralysis and lagophthalmos.

Immunology of Leprosy

Not all leprosy infections result into development of leprosy disease. The occurrence is dependent one's immunity. There are two types of immunity;

1. Humoral Immunity" or Antibody Mediated Immunity and
2. Cell-Mediated Immunity" (CMI).

Humoral immunity

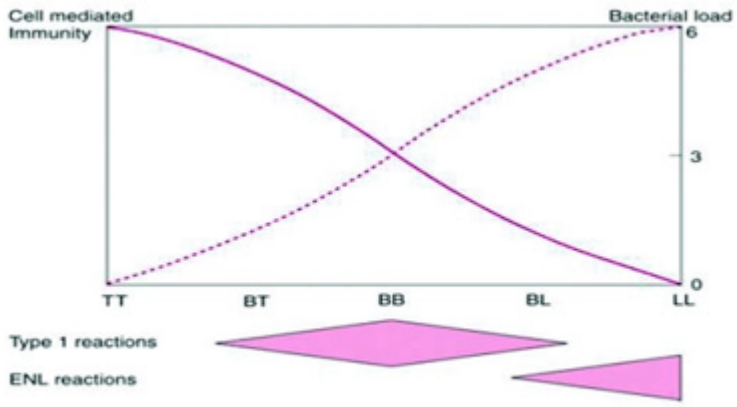
In humoral Immunity, certain chemicals (antibodies) are generated by the body when it is invaded by antigens. In certain types of infection, antibodies are effective in cleansing the system of the toxins liberated by the invading organism. However, while humoral Immunity is very effective in fighting many forms of infection, it is has little effect against M.leprae and can in fact cause much suffering through mediation of type 2 leprosy reaction.

Cell-Mediated Immunity (CMI)

Some of the invading foreign bodies and their antigens stimulate the production of certain special defense cells, at the same time establishing an inflammatory reaction. Cell-mediated immunity is essential for the body's defense against such diseases as tuberculosis, and leprosy. Where the antigens accumulate, immune cells mainly lymphocytes collect at the site. In the case of leprosy, these are mainly the peripheral (cooler) nerves and, more particularly, the nerve's Schwann cell. M.leprae has an affinity for the cooler areas of the body and this characteristic has a bearing on the types of deformities that result from the invasion of M.leprae.

The smaller lymphocytes, have no phagocytic property therefore cannot ingest/digest the M. leprae, like the macrophages. The role of the lymphocytes is to secrete certain chemicals which attract the larger macrophages to the site of antigen build-up and assist the macrophages to engulf and digest the M.leprae. Cell-Mediated-Immunity (CMI) is the protective immunity that the body needs against leprosy. Majority of the humans have this type of immunity however in varying degrees.

At one end of the "Immunological Spectrum" leprosy patients with a well-established CMI have the form of the disease known as "Tuberculoid" leprosy, but they may have little Humoral immunity. At the other end of the Immunological Spectrum, Lepromatous leprosy is a complete opposite with a well-established Humoral Immunity but no CMI. The latter is the infectious form of leprosy the multibacillary leprosy.



Immunological spectrum and classification of leprosy

Although immunity, in most cases, helps the body's defenses against the invasion of bacteria and their antigens, there are occasions when the body reacts violently to the M. leprae antigens. This is called the "Lepra Reaction". Reactions in leprosy are of several types: "Type 1" and "Type 2"

Immunological Response and Deformity

Although tuberculoid leprosy patients, with strong CMI, may have few bacilli in their bodies that they cannot be detected by ordinary microscopy, they may suffer severe nerve damage due to the massive lymphocytic response, causing the nerves to swell 5 or more times the normal size.

On the other hand, Lepromatous, infectious patients, whose bodies may be teeming with millions of M.leprae, may suffer relatively little nerve damage (in the early stages), because the lack of CMI means that there is no strong build-up of defense cells around the nerves. Leprosy is a very enigmatic disease. Although it can look to be a highly contagious disease, in actual fact, of all the communicable diseases, Leprosy (the tuberculoid type) is the least contagious.

Classification of Leprosy

There are two main classifications of leprosy disease based on two criteria;

1. The number of lesions as recommended by WHO
2. Immunological and clinical features as per the Ridley Joplin classification

WHO

WHO classifies leprosy into two groups for epidemiological and treatment reasons.

Pauci-bacillary leprosy:

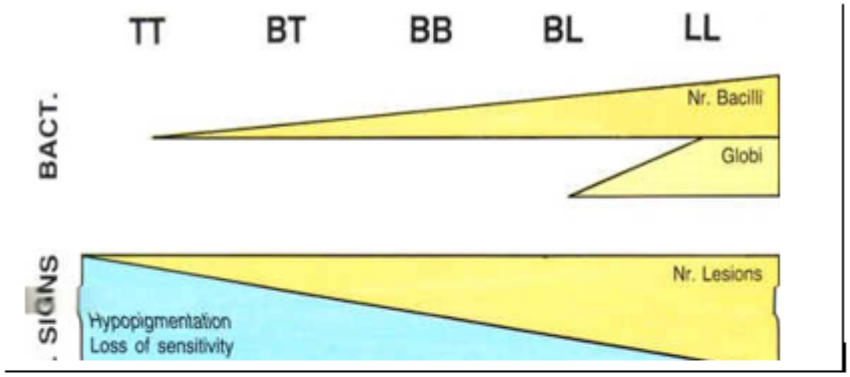
- Patients with 1 to 5 hypo pigmented patches
- Skin smears negative

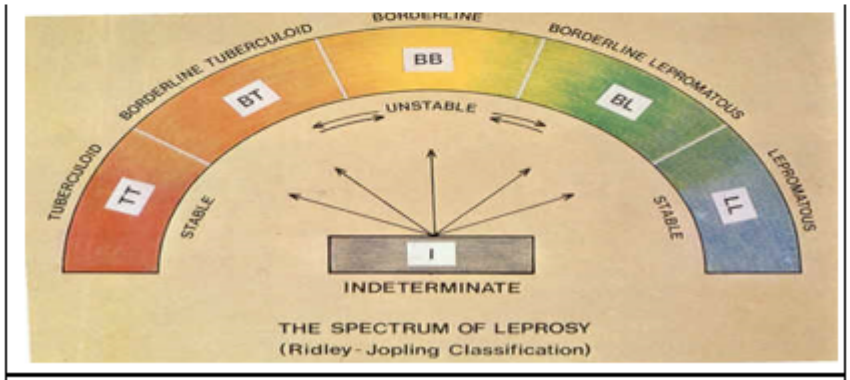
Multi-bacillary leprosy (MB)

- Have more than 6 patches Skin smear often positive
- Patients with MB leprosy may present with plaques, macules, papules and or nodules with skin infiltration. Patients with neural leprosy are classified and treated as MB leprosy

Ridley and Joplin Classification

Leprosy is classified into six types based on the clinical features (Ridley & Joplin classification). The type of the disease is a reflection of the immune status of the host.

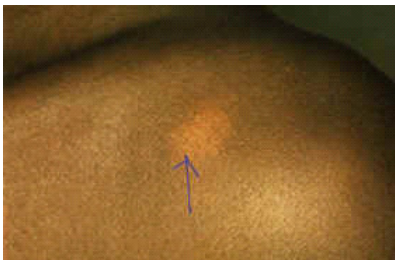




Leprosy disease spectrum as per Ridley Joplin classification

Indeterminate leprosy

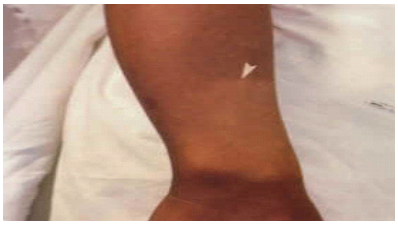
A single symptomless lesion characterized by hypo-pigmented spots. The lesion undergoes spontaneously healing.



Indeterminate leprosy patch

Tuberculoid leprosy (TT)

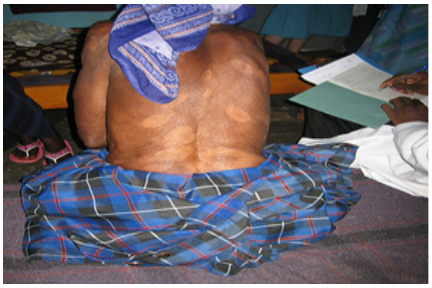
Usually a single patch with well-defined raised borders or a large hypo pigmented asymmetrical lesion. Lesion is dry and hairless, infectivity is minimal at this stage loss of sensation is seen. Few nerves become thick followed by loss of function. Skin smears are negative and may spontaneously get cured.



Tuberculoid leprosy lesion

Borderline Tuberculoid leprosy (BT)

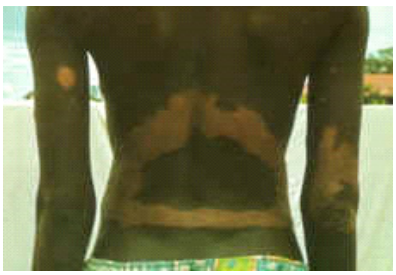
BT leprosy is characterized by numerous skin lesions with less well defined margins and satellite lesions. The disease goes back to the tuberculoid stage or without treatment may progress to BB. There is usually early nerve damage. Skin smears are negative.



Multiple lesions on the back, some of the lesions Central healing

Borderline Borderline leprosy (BB)

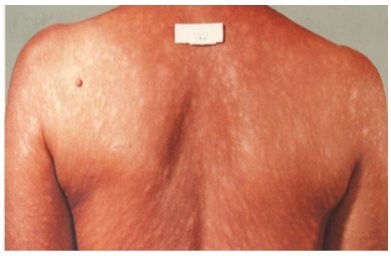
Several small and irregular punched out lesions are seen moderate sensory loss is seen. This is a very unstable form of leprosy with a high likelihood of either going back to the previous stage or progressing to the next stage. Nerve damage and deformities are very common and skin smears are positive.



Borderline borderline leprosy lesion

Borderline Lepromatous leprosy (BL)

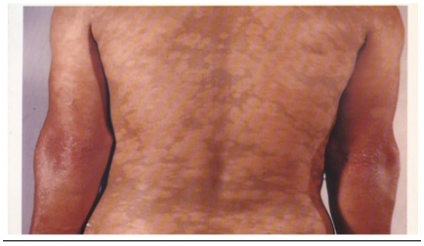
Several lesions such as, ill-defined macules, plaques, papules, and nodules are seen. The nodules tend to affect the lower parts of the ear lobes. Patients present with lateral madarosis. There is early nerve involvement.



Above -Borderline Lepromatous, ill-defined macules
NB- For this client there was no sensory loss in the patches

Lepromatous leprosy (LL)

Early symptoms include several lesions such as plaques, macules, papules, and nodules. Nasal congestion, discharge and bleeding is seen. Inflammation of the leg and ankles. Progressive symptoms include thickening of the skin (skin infiltration) in the foreheadand ear lobes loss of eyebrows and eyelashes. Nodules in the legs break and form ulcers. Skin lesion begin as vaguely erythematous or hypo pigmented macules often on the lower back without itch or pain. The skin smears is always positive with late nerve damage.



Above – Lepromatous leprosy

Leprosy Management

Chemotherapy

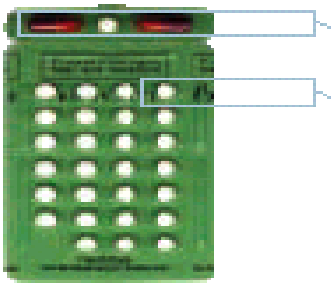
Multiple drugs (Multiple Drug Therapy -MDT) are used in treatment of leprosy. There are 3 first line drugs used in leprosymanagement; Rifampicin, Clofazimine and Dapsone.

Treatment of leprosy among children.

Treatment of leprosy among under 15 years for PB leprosy and MB leprosy is as follows.

Treatment of Leprosy in Adults

The following drugs are used in leprosy treatment among adults.



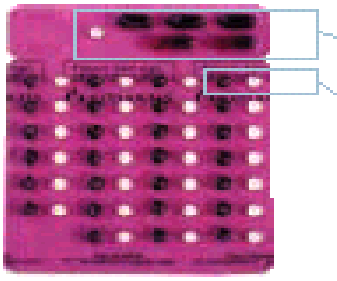
PB adult blister pack

PB adult treatment:

Once a month: Day 1
– 2 capsules of rifampicin (300 mg X 2)
– 1 tablet of dapsone (100 mg)

Once a day: Days 2–28
– 1 tablet of dapsone (100 mg)

Full course: 6 blister packs



MB adult blister pack

MB adult treatment:

Once a month: Day 1
– 2 capsules of rifampicin (300 mg X 2)
– 3 capsules of clofazimine (100mg X 3)
– 1 tablet of dapsone (100 mg)

Once a day: Days 2–28
– 1 capsule of clofazimine (50 mg)
– 1 tablet of dapsone (100 mg)

Full course: 12 blister packs

Note;
Children under 10 years of age should receive appropriately reduced doses of drugs, such as

- Rifampicin: 10mg/kg body weight once a month.
- Dapsone; 2 mg /kg body weight per day
- Clofazimine; 1 mg / kg body weight to be given on alternate days, depending on the dosage.

Common Drug Side Effects and Management

Dapsone

Slighting itching (Dapsone syndrome)

Reassure patient and treat symptomatically with an anti-histamine.

Anaemia

Investigate for other causes of anemia, and manage appropriately/ refer to medical officer or TB/Leprosy coordinator for further management.

Exfoliative dermatitis

The skin is itchy, and later peels off. The patient is usually very ill. Stop drugs immediately and refer the patient to medical officer or SCTLC or nearest hospital.

Fixed drug reaction

Stop drugs, the eruption will slowly clear after stopping.

Clofazimine (Laprene)

Gastro intestinal disturbances nausea,vomiting, abdominal pains.
Give drugs after meal.

Red skin/eyes

The patient has no complaints at all apart from the cosmetic effect. This is a harmless condition, reassure the patient and continue treatment

Rifampicin

Red urine

Harmless, no action needed. Reassure the patient and continue treatment.

Symptoms as for severe flu

Treat symptomatically and reduce the dosage to half until the symptoms have disappeared

Jaundice

Stop all drugs immediately and refer patient to a medical officer or SCTLC

Anaemia

Investigate for other causes of anemia, manage appropriately/ refer to medical officer or SCTLC for further management.

Leprosy Reactions

Immunology of leprosy

Care and Support

- Include VMT/ST
- Disability grading
- Do the Baseline investigations.

Leprosy Reaction

This results from of exaggerated immune response to body tissues due to the invasion by *M. leprae.* Leprosy reactions are classified into two categories:

- Type 1 leprosy reaction
- Type 2 leprosy reaction

Type 1 leprosy reaction

- *Skin*: inflammation in the skin patches, swelling, redness & warmth. Patches usually not painful. Occurs early: 6 months treatment
- *Nerves*: tenderness of nerves and loss of function, closing the eyelid may be affected, but the eye itself is not.

- *General Systemic Involvement:* inflammation is localized in the skin and nerves, the person do not feel too ill and no fever.
- Common in patients with TT, BT, BB and BL.

Type 2 leprosy reaction

- *Skin*: new painful subcutaneous nodules in the face, trunk, upper and lower extremities. Lesions are painful and erythematous (ENL).
- ENL nodules can be mild, transient or severe. If very severe they can break and form ulcers with secondary bacterial infection (*Lucio phenomenon*) a life threatening condition.
- Leprosy nodules are superficial on the skin and not painful.
- Common in patients with, BB, BL and LL
- *General systemic involvement*: Eye damage results in Iridocyclitis and blindness.
- *Testes*: a hormonal imbalance: gynaecomastia, loss of libido, impotence and infertility.
- Lymph nodes: will be enlarged and tender- lymphadenopathy.
- Hand and feet: bone necrosis and deformities.
- Kidney: - nephritis.
- Liver and spleen: - hepato-spelomegally

Differential diagnosis of leprosy reaction

- *hDrug reactions*: not common; usually accompanied by itching, which is not a typical feature of leprosy reactions
- *Other causes of inflammation*: signs on the skin not correspond with leprosy patches, mostly flat lesions with hyper pigmentation.
- *Local sepsis*: will generally be localized to just one part of the body and the cause may be obvious e.g. wound or insect bite.

Factors predisposing to leprosy reaction

- *Antileprosy treatment*: improved immunity & Ag-Ab complexes.
- *Intercurrent infection*: disrupt immunological balance between bacilli and host.

Physiological factors:

- Stressful conditions due to stigma.
- Pregnancy.
- Puberty in males due to hormonal changes.

Management of leprosy reactions

Management of type 1 reactions is divided into 3 categories:

1. *Mild* type 1 reactions,
2. *Moderate* type 1 reactions
3. *Severe* type 1 reactions

Management of Type 1 Reaction

Mild type 1 reaction

- A mild type 1 reaction is occurs in the skin only; there may be mild fever and slight swelling (edema) of the limbs.
- *Treatment*- do baseline VMT/ST, paracetamol 2 tabs TDS for 1 week and review after 1 week
- If there is deterioration to moderate or severe, treat as recommended.

Moderate type 1 reaction

- *Moderate type 1 reaction* – a number of skin patches are involved, some of the nerves are enlarged and tender but no evidence of loss of function.
- *Treatment* – Paracetamol, 2 tabs TDS for 2 weeks and Chloroquine 2 TDS for 2 weeks. Clinical review the patient, do VMT/ST
- If there is deterioration to severe, treat as recommended

Severe type 1 reaction

Most of all the skin patches are affected, A number of nerves are enlarged, tender, with evidence of loss of nerve function

Treatment – Admit and start long course Prednisolone, do 2 weekly VMT/ST as you monitor

Start with 40mg OD for 2 weeks

30mg OD for 2 weeks

20mg OD for 6 weeks

1. If there is no response or no changes in the VMT/ST. The treatment has failed.
2. Wean the patient off Prednisolone by reducing to 15mg OD for 2 weeks, 10mg OD for 2 weeks and 5mg OD for 2 weeks.
3. Assess for reconstructive surgery, rehabilitation and health education on the care of the eyes, hands and feet.
4. At 20mg OD 6 weeks, and after 6 weeks of prednisolone, VMT/ST still shows improvement in nerve function.
5. Continue with 20mg Prednisolone daily and 2 weekly VMT/ST until you get 3 readings of VMT/ST that are similar.
6. Reduce Prednisolone to 15mg OD for 2 weeks, 10mg OD for 2 weeks and 5mg OD for 2 weeks.

Management of type 2 reaction

Management of type 2 reactions is divided into 4 categories:

1. *Mild* type 2 reactions,
2. *Moderate* type 2 reactions
3. , *Severe* type 2 reactions
4. *Chronic* type 2 reactions.

Mild type 2 reaction

- In a mild type 2 reaction normally the patient has transient ENL nodules; there is no nerve or systemic involvement.
- Treat as outpatient with paracetamol 1 gm 8 hourly for 7 days, review and act appropriately

Moderate type 2 reaction

- These patients have generalized ENL with mild fever.
- Treat with paracetamol at 1 gm 8hourly for 2 weeks as an outpatient, review every week and act appropriately.

Severe type 2 reaction

- There is generalized ENL, high fever (30-40°c) and systemic involvement of organs.
- Put patient on short course prednisolone:
- Start at 60mg OD for 3 days then
- 40mg OD for 3 days then
- 30mg OD for 3 days then
- 20 mg OD for 3 days then
- 15 mg OD for 3 days then
- 10 mg OD for 3 days then

  5 mg OD for 3 days.

Chronic (recurrent) type 2 reaction

- Treatment requires reinitiating of the short course steroids together with Clofazimine at a dose of 100mg 8hourly for 1 month then 100mg BD for a month then 100mg OD for 1 month.
- Thalidomide may be given instead of Clofazimine for duration of 4 months.

The eye in leprosy

- The eye is affected in leprosy in 2 main ways: direct bacillary invasion & leprosy reactions.
- Direct bacillary invasion: leads to a leproma, and exposure keratitis..
- Bacillary invasion of the cornea: leads to vascularization of the cornea resulting in opacities and blindness.
- *Management*: initiation of MDT.

Type 1 reaction in the eye

Type 1 reactions: facial nerve damage leads to inability to close the eye (lagophthalmus)

- This results in exposure keratitis which leads to opacities & blindness. It exposes the eye injuries by foreign objects, infections, fibrosis and blindness.
- If the eyes are not active the muscle of obicularis oculi atrophy leading to *Entropion*

- Damage to the trigeminal nerve is associated with loss of blink reflex leading to exposure keratitis and blindness as discussed above.
- There is also loss of corneal sensation which leads to unnoticed injury of the cornea and secondary bacterial infection and ultimately blindness.
- Deposition of Ag-Ab complexes into the cilliary body leads to acute inflammation (Iridocyclitis).
- Iridocyclitis leads to increased intraocular pressure (Glaucoma) which can lead to damage of the retina and blindness.
- Glaucoma comes as result of anterior and posterior synechiae

Management of the eye

- Iridocyclitis: *Initial care:* Instill atropine eye drops into the eye, Pad the eye, Refer a patient for admission and further management.
- *Inpatient care:* A patient should receive an ophthalmologist review where available.
- Atropine sulphate drops relaxes the iris muscle relaxes making them shorter thus reducing the risk of attachment
- Deposition of Ag-Ab complexes into the cilliary body leads to acute inflammation (Iridocyclitis).

Signs and symptoms of Iridocyclitis

1. Perilimbal redness of the cornea
2. Pain in the eye
3. Blurred vision
4. Photophobia
5. Constricted pupil with poor reaction to light
6. In recurrent attacks of type 2 reaction the patient may develop premature cataract

Management of the eye

- Iridocyclitis: *Initial care:* Instill atropine eye drops into the eye, Pad the eye, Refer a patient for admission and further management.
- *Inpatient care:* A patient should receive an ophthalmologist review where available.
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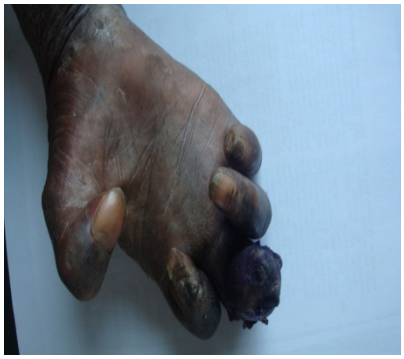
Causes of deformities in leprosy include:

- *M. leprae* invasion: poor impulse transmission
- Loss of sensation: unnoticed injuries
- Dryness: cracking, wounds, and infection
- Paralysis: wasting, disuse, poor posture or improper handling of objects.
- Mechanical injuries: from working tools, wrong footwear and general injuries.

Common deformities & disabilities

- Madarosis- loss of eyebrows and eye lashes
- Lagophthalmus- leads to inability to close and open the eye voluntarily.
- Collapsed nose (saddle nose)- leads to poor breathing in and out
- Wrist drop – inability to extend the wrist
- Ape thumb- leads to no thumb opposition and abduction
- Claw hand – inability to flex the proximal metacarpophalangeal joint of the 4th and 5th fingers and inability to extend the distal metacarpophalangeal joints of these fingers
- Foot drop – inability to dorsiflex and evert the foot
- Claw toes – leads to injuries to the metatarsal heads and toes
- Plantar ulcers



Special cases and their treatment

Treatment during pregnancy and breast-feeding

The standard MDT regimens are safe, both for the mother and the child and therefore should be continued during pregnancy and breast-feeding.

Treatment for patients also infected with HIV

Patients infected with HIV usually respond equally well to leprosy treatment as those without HIV infection.

Treatment for patients with Leprosy and TB

Patients suffering from both TB and leprosy require standard TB treatment in addition to the standard MDT. Hence, skip the monthly dose of rifampicin in the leprosy MDT regimen. Once the TB treatment is completed, the patient should continue his/her MDT, or the other way round.

Interaction between HIV and leprosy

Most of the recent epidemiological, clinical and pathological studies show neither an increased HIV prevalence among leprosy cases, nor an alteration in the clinical spectrum of leprosy among co- infected patients, however there is some evidence that immune mediated reactions (particularly type 1) occur more often in co- infected patients. In the year 2014, among the 133 cases notified, 45 % (60 clients) were tested for HIV, co- infection rate was at 3.3% (2 clients).

Having both leprosy /TB/HIV

- Manage all of them.
- LEPROSY -600mgs

- Rifampicin- 0-5 ….150mg
- 6-14….. 300mgs
- Monitor blood for Thrombocytopaenia in patients on 2nd line ART
- Consider super-boosting Kaletra during the treatment period, after Leprosy treament, revert to normal doses of Kaletra
- If available, consider using Rifabutin as an Alernative to Rifampicin 600mg

Leprosy and Malnutrition

(For further information, refer to the nutrition section in main document)

- Do Nutritional assessment
- Manage as per nutritional interventions
- Vitamin A
- Pyridoxine
- Food supplements if the BMI is 16.5 or LESS
- BMI of 18.5 or >, provide nutritional counseling to the client

Leprosy Relapse

A patient should be diagnosed as a "relapse" if he/she has previously completed a full course of MDT and returns 2 years later with signs of active leprosy (of the same classification as the original classification) requiring chemotherapy. Relapses after a complete course of MDT are very rare. A patient who has MB disease after being treated as a PB case is a mis-classification and has to start MB treatment (section 3.2.5).

One or more of the following signs are indications of a relapse:

- Active skin lesions: appearance of new skin lesions. Increased erythema (redness) in previously existing lesions.
- New nerve lesions: enlargement and/or tenderness of one or more nerves which were previously normal.

Rehabilitation

Physical

- This involves physical exercises, sometimes in line with pre and post operation management of leprosy.
- It also includes vocational training and fabrication of adaptive aids.
- Patients are encouraged to participate in recreational activities such as reading and indoor games.

Economic empowerment

- Leprosy patients are encouraged to form groups and start income generating activities.
- Those with vocational skills are supported to establish or start trades
- that will make them self reliant.

Spiritual

- It helps in reducing stigma

Surgical

This involves surgical procedures to correct the deformities:

- **Madarosis**: Hair grafting
- **Lagophthalmos**: Tarsorraphy &Temporalis muscle tendon transfer (TMT)
- **Nasal collapse**: Postnasal inlay graft
- **Wrist drop**: Wrist arthrodesis
- **Ape thumb**: Opponens plasty
- **Claw hand**: Extensor to flexor 4 tail graft, Sublimis muscle transfer.
- **Foot drop**: Tibialis posterior muscle transfer (TPT).
- **Plantar ulcers**: Trans-metatarsal head resection,
- Skin grafting,
- Sequestretomy,
- Fore foot amputation,
- Symes amputation, Below-knee amputation
- (BK), Above-knee amputation (AK),
- Through-knee amputation (TK)
- Orthopedic appliances
- Footwear: normal tyre sandal with micro-cellular rubber (MCR)
  - Plasterzote sandal
  - Plasterzote boot
  - Elephant boot
  - Peg leg
  - Below-knee prosthesis
  - Above-knee prosthesis

Prevention of Leprosy

a) Chemo-prophylaxis

   Unlike TB, there is no indication for chemoprophylaxis for Leprosy

b) BCG

   BCG vaccination has a documented and substantial effect in preventing leprosy and is therefore considered as an important tool for leprosy control

c) Health education

d) Early diagnsis, Prompt and adequate treatment

Monitoring and Evaluation

Key indicators for monitoring progress

- Number and rate of new cases detected per 100,000 populations per year.
- number and rate of new cases with G2D detected per million population per year
- Treatment completion /cure rate for MB cases

Other indicators for monitoring progress

- Number and rate of new cases detected per year among persons less than 15 years of age per 100,000 populations under 15 years of age.
- Proportion of G2D cases among new cases
- Proportion of female among new cases
- Proportion of MB cases among new cases
- Proportion of household contact cases among new cases

Indicators for evaluating the quality of services including diagnosis, treatment and disability care:

- Prevalence of G2D per million population (G2D in new patient and in those who have completed MOT)
- Proportion of new cases verified as correct diagnosed
- Prevalence detection ration
- Number of relapse among those who have completed MDT
- Number of patients assessed and completion of treatment

CHAPTER 5

LABORATORY DIAGNOSIS OF TB AND LEPROSY

Introduction

Laboratory services play a key role in TB and leprosy diagnosis, prevention and control in Kenya. Smear microscopy (both light and fluorescence), molecular techniques (Line Probe Assay and Xpert MTB/RIF) and culture (solid and liquid media) are all available in the country for TB and MDR TB diagnosis. Both the NTLD Program and the National TB Reference Laboratory (NTRL) coordinate diagnostic services, while a laboratory technical working group guides in implementation of TB laboratory services. TB and leprosy diagnosis is embedded in various national guidelines.

Diagnosis of Tuberculosis is achieved through the provision of microscopy, Genexpert, mycobacterium culture and Drug Susceptibility testing (DST), and by PCR/DNA sequencing methodologies. The Laboratory has established a network to ensure that diagnosis is accessible by providing different tests at different levels of service delivery. The laboratory network has a pyramid structure based on a large number of Level 1 laboratories accessible to all presumptive PTB cases and TB patients, a moderate number of level 11 laboratories located in mid-sized population centres and health facilities and a few apex level 111 laboratories at the county, national level.

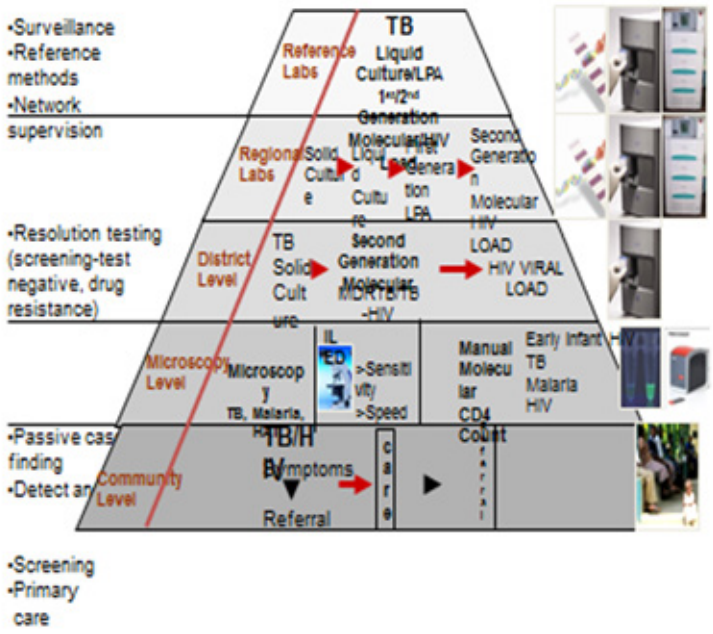
In the Public sector NTRL, IOM and KEMRI CDC Kisian carry out both culture and DST. All these facilities are supervised by NTRL for purposes of maintaining quality.

Specimen collection

Sputum

For good quality specimens to be obtained, patients must be instructed on how to produce sputum. Specimens should be collected in a well-ventilated space or preferably outdoors. The patient rinses the mouth with water and then takes a deep breath and then coughs to expectorate sputum directly into a wide-mouthed, unbreakable, leak proof container and closes the lid tightly. Label each specimen with the patients name as it appears on the laboratory request form.

Figure 5.1: Placement of Diagnostic Tools



Specimen other than sputum (SOTS)

Laryngeal swab

Laryngeal swabs may be useful in children and patients who cannot produce sputum or may swallow it.

- Collect laryngeal swabs in the early morning, before patients eat or drink anything.
- Use a sterile absorbent cotton swab for collection.
- Transport each specimen in a container with a few drops of sterile 0.9% saline solution in order to keep the swab wet.

Other respiratory specimens

Trans bronchial and other biopsies taken under sterile conditions should be kept wet during transportation by adding few drops of sterile 0.9% saline to the tissue.

Note: Specimens are sometimes sent in formalin or bleach! It may therefore be advisable to remind the physician of collection conditions, the day before surgery.

Gastric lavage

Gastric lavage often contain MOTT and are therefore rarely used for adults; they are indicated for children, however, who produce almost no sputum

Make the collection early in the morning, when the patient has an empty stomach.
Neutralize the specimen by adding 100 mg of sodium bicarbonate to the gastric aspirate and transport it immediately to the laboratory.

Extrapulmonary specimens

The laboratory may receive a variety of specimens for diagnosis of extrapulmonary TB – body fluids, tissues, urine etc. These specimens may be broadly divided into two groups which are processed in different ways:

Specimens collected from sterile sites

These include spinal fluid, pericardial, synovial and ascitic fluid, blood, bone marrow, etc., which are usually free from contaminating flora.

a. All liquid specimens should be collected in sterile glass containers without using any preservative.
b. Specimens can be inoculated directly into liquid vials and transported to the laboratory for culture.
c. Specimens must be transported to the laboratory immediately; they should be processed as soon as possible or kept at 2–6 °C.

Specimens collected from non-sterile sites

a. A urine specimen should consist of a single, early-morning, midstream sample.
b. Skin tissues, pus swabs and pus aspirates

Note: Stool samples should be discouraged; however, stool samples from immunocompromised patients may be used, mainly to detect MOTT.

Table 5.1: Table Showing Specimen Collection and Handling Procedures

Test	Specimen Type	Type of container	Specimen volume	Transport /strorage conditions
Microscopy	Sputum, CSF, Aspirates, Biopsies, Pus/ swabs	a wide-mouthed, unbreakable, leakproof container	3-5ml	2-6°C
MTB Rif Assay (Gene Xpert)	Sputum, CSF, Gastric aspirate, Nasopharyngeal aspirate, Pleural fluid,Pericardial fluid, Ascetic fluid, FNA, Lymph node biopsy, (Stool for children)	50ml falcon tubes	2-3ml	2-6°C
TB culture / DST	Sputum, CSF, Aspirates, Biopsies, plural effusions, urine, **Laryngeal swab**, gasric larvage pus swabs	50ml falcon tubes 28ml sterile universal bottles	Bronchial secretion (2–5 ml) , BAL (20–40 ml) Pleural effusions (20–50 ml) CSF-(3ml) Urine-(200ml)	2-6°C

LPA	Sputum, CSF, Aspirates, Biopsies, plural effusions, urine, laringeal swabs, gastric larvage pus swabs,	50ml falcon tubes 28ml sterile universal bottles	As for culture	2-6°C
Pregnancy test	Urine	Wide mouthed, unbreakable, leakproof container.		
LFTs (AST, ALT, Bilirubin)	Serum	Red top, Plain tube	4ml	RT
Full hemogram	Whole blood	EDTA(Purple top tube)	4ml	RT
CD4	Whole blood	Green top tube	4ml	RT
TSH	Serum	Red top/Plain tube	4ml	RT
Creatinine, Potassium & Magnesium	Serum	Red top/Plain top	4ml	RT
Viral Load	Whole blood	Purple top	4ml	2-8

Request Forms

The request forms must be filled by the clinician handling the patient.

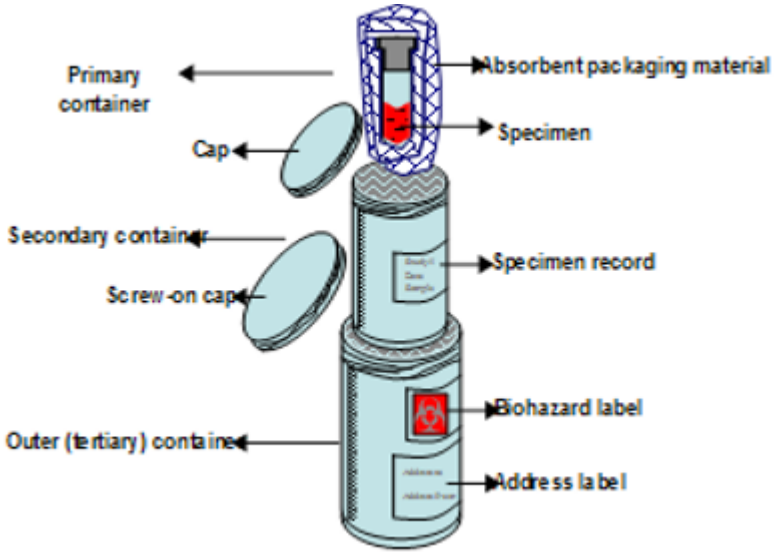
The following information must be clearly indicated:

- Name (all three names)
- TB registration number
- IP/OP number
- Address
- Actual age of patient
- Sex of patient
- Referring clinic or ward
- Type of specimen
- Date of collection
- Clinician's name and signature
- Examination required: specify whether for smear, culture or sensitivity
- Type of patient: Tick the correct type of patient
- Previous treatment: Indicate the duration of treatment and drugs used.

Transport and Packaging

The basic packaging system for local surface transport of all specimens consists of triple packaging systems.

Figure 5.2: Packing & shipping infectious Materials



Transport conditions

Specimens collected should be transported to the laboratory as soon as possible. If a delay of a few days cannot be avoided, keep specimens cool (refrigerated but not frozen) Up to a week in cold conditions will not significantly affect the positivity rate of smear microscopy; however, the additional growth of contaminants will result in an increased contamination rate on culture media.

Sample Rejection Criteria

Quality specimen is a key to quality results hence, samples should be rejected when;

- The request form is not received with the specimen
- There is a mismatch of information details on the request form with details on the specimen container.
- Container used is not appropriate
- Specimen unlabeled
- Specimen container broken
- Specimen container leaked
- Specimen volume not sufficient
- Specimen not appropriately packed

Laboratory Diagnosis Methodologies for Mycobacteria

1. Microscopy

This is one of the tools used to diagnose TB more especially in resource limited countries. Smear Microscopy is either ZN or FM/ LED. Flourescent microscopy is more sensitive compared to the ZN method. A spot and a morning sputum sample is collected from

presumptive PTB cases while follow up smears are done at month 2, 5 and 6.Specimen other than sputum (sots), are collected from presumptive EPTB cases for diagnosis according to the NTLP guidelines.

2. Molecular Technology

i) GeneXpert

The National Tuberculosis, Leprosy and Lung Disease Program, on behalf of the Ministry of Health of Kenya, has been implementing the use of new technologies for diagnosis of TB including Fluorescent microscopy as well as XpertMtb/Rif assay which is an automated molecular test. This has been done alongside quality systems in place to ensure reliability of test results. The use of XpertMtb/Rif has made the turnaround time for Tuberculosis diagnosis and detection of rifampicin resistant to be short enabling efficient patient management.

Indications of Gene Expert

Low risk for DR TB

All presumptive TB cases who are not in the high risk group including:

- People Living with HIV with TB symptoms
- Children <15 years with TB symptoms
- All presumptive TB cases with a negative smear microscopy result

High risk for DR TB

- Previously treated TB patients: treatment failures, relapses, treatment after loss to follow up
- Drug Resistant TB patient contacts
- TB patients with a positive smear result at month 2 or month 5 of TB treatment
- Patient who develops TB symptoms while on IPT or has had previous IPT exposure
- Healthcare Workers with TB symptoms
- Prisoners with TB symptoms
- Refugees with TB symptoms

Note: Genexpert test is the preferred first test for TB diagnosis and identification of rifampicin resistance in all presumptive TB cases*
Patient's diagnosed using genexpert should be followed up using smear microscopy

In situations where genexpert is not available, smear microscopy may be used for initial TB diagnosis and concurrently, a sample specimen sent for genexpert test.
Insert Algorithm

Expected Results

These results are sent to the clinician for patient management No MTB detected

- MTB detected No Rif resistance
- MTB detected Rif resistance

These results are sent to the clinician and a fresh specimen is requested for repeat

- MTB detected Rif resistance Indeterminate
- Invalid
- Error
- No results

Managing Genexpert Discordant results

1. Smear-**Negative** microscopy vs. MTB **detected** by Xpert
    - Will be common
    - RIF Resistance detected –
        - collect sample for culture & DST ,
        - Start treatment with cat iv
    - RIF resistance not detected –
        - collect sample for culture & DST for the surveillance group
        - Start treatment with cat 1
        - RIF resistance indeterminate- repeat GeneXpert but emphasize on (quality sample) proper sample collection

2. Smear-positive microscopy vs. MTB **not detected** by Xpert
    - Will be rare
    - Lab error
    - Repeat both sputum microscopy and Gene Xpert
    - Consider **Non Tuberculous** Mycobacteria

ii) Line Probe Assays

Conventional methods for mycobacteriological culture and drug susceptibility testing (DST) are slow and cumbersome, requiring sequential procedures for isolation of mycobacteria from clinical specimens, identification of Mycobacterium tuberculosis complex, and in vitro testing of strain susceptibility to anti-TB drugs. During this time patients may be inappropriately treated, drug resistant strains may continue to spread, and amplification of resistance may occur. Novel technologies for rapid detection of anti-TB drug resistance have therefore become a priority in TB research and development, and molecular line probe assays focused on rapid detection of rifampicin resistance (alone or in combination with isoniazid) are most advanced.

Line probe assay technology

DNA is extracted from M. tuberculosis isolates or directly from clinical specimens. Next, polymerase chain reaction (PCR) amplification of the resistance-determining region of the gene under question is performed using biotinylated primers. Following amplification, labelled PCR products are hybridized with specific oligonucleotide probes immobilized on a strip. Captured labelled hybrids are detected by colorimetric development, enabling detection of the presence of M. tuberculosis complex, as well as the presence of wild-type and mutation probes for resistance. If a mutation is present in one of the target regions, the amplicon will not hybridize with the relevant probe. Mutations are therefore detected by lack of binding to

wild-type probes, as well as by binding to specific probes for the most commonly occurring mutations. The post-hybridization reaction leads to the development of coloured bands on the strip at the site of probe binding and is observed by eye.

All samples sent for culture and DST and are smear positive are done line probe assay to detect the presence of MTB Complex and resistance pattern of rifampicin and isoniazid.

3. Culture and Drug Susceptibility Testing

NTLD-P policy for culture targets high risk groups for identification of drug resistant TB as categorized below;

- Smear positive relapse
- Smear negative relapse
- Failure first line treatment
- Failure retreatment
- Lost to follow up
- DR-TB contact
- DR-TB follow ups
- Health care worker

Culture methods provide definitive diagnosis by establishing the viability and identity of the organisms and allow the detection of drug resistance. A good sputum specimen consists of recently discharged material from the bronchial tree, with minimum amounts of oral or nasal material. **Satisfactory quality implies the presence of mucoid** or **mucopurulent** material and is of greater significance than volume. Ideally, a **sputum specimen** should have a volume of approximately **5ml**,although smaller quantities are acceptable if the quality is satisfactory. NTRL has established a testing alogarithm to guide the detection of DRTB.(see annex). All culture positive samples are identified for MTB Complex followed with a DST. Smear negative cases that turn to be culture positive are identified and subjected to DST and also Line probe assay .

Secondline DST should be done for all DR TB patients at baseline ,six months later and any time there is a positive culture in a previously culture negative DR TB followup case.

M. tuberculosis requires an enriched medium for culture. It grows slowly and takes **three to six weeks** or **longer to give visible colonies**.

Mycobacteria Other Than Tuberculosis (MOTT)

These refer to all the species in the family of mycobacteria that may cause disease, other than the Mycobacterium tuberculosis (TB)complex [i.e. M. tuberculosis, M. africanum, M. bovis, M. canettii, M. microti, M. caprae, M. orygis, and M. pinnipedii and M. leprae which can cause Hansen's disease (leprosy).

MOTT are isolated in LJ medium and liquid medium.

Different species are identified by PCR and DNA sequencing methodology and reported to the clinician for patient management.

Most common MOTT species are M.*abscessus*, M.*kansasii* and M.*intracellulare.*

Leprosy

The diagnosis of leprosy is based on any of the three cardinal signs

- Hypo pigmented skin patch with loss of sensation.
- One or more enlarged peripheral nerves
- The presence of Leprosy bacilli

Where available laboratory tests may be used to confirm the diagnosis of leprosy. These include:

- Bacteriological
- Histological
- Molecular methods
- Bacteriological

Slit skin smears

Smears can be taken from the areas of the body that manifest leprosy like a patch a nodule area of anesthesia or infiltration. In practice smears are commonly taken from ear lobes, one elbow, and a contra lateral knee. These smears are stained with ZN and examined for the presence of Acid Alcohol Fast Bacilli (AAFBs).

Histology

Skin or nerve biopsies can be taken for histological examination using various histological techniques like, ZN, FITES,etc

Laboratory Infection Prevention Control

Specimen processing in the laboratory must observe at minimum key standards of biosafety. Key areas which must be taken care of include;

- Transmission of TB bacilli
- Risk assessment and precaution levels

- Safety practices in the TB microscopy laboratory and the Xpert MTB/RIF laboratory
- Safe disposal of infectious waste

Following laboratory biosafety procedures prevents laboratory staff from becoming infected with TB and prevents microorganisms from being released into the environment. Specialized equipment may aid good laboratory practice but does NOT replace it. **Always wear gloves and laboratory coats when handling samples from patients.**

The main risks in a TB laboratory are related to the aerosols generated during the procedures that could be inhaled by laboratory workers. The risk of aerosolization is associated with the:

- Type of procedure
- Frequency of testing, and the laboratory's workload
- Consistency of the material and its predisposition to aerosolize (for example, viscous liquids versus dry solids) Bacillary load of the materials.

Classification of laboratory activities:

1. Smear preparation and staining: [Dirty activity]
2. Processing samples for Xpert MTB/RIF testing, and inoculating cartridges: [Dirty activity]
3. Microscopic examination of stained smears: [Clean activity]
4. Loading cartridges into the GeneXpert instrument: [Clean activity]
5. Record keeping and storage: [Clean activity]

Safety practices Air flow

Use of bench spaces: The bench used to process specimens for direct sputum-smear microscopy or the Xpert MTB/RIF assay should be separate from areas where specimens are received and from areas where paperwork is completed and telephones are used.

Ventilation: When appropriate microbiological techniques are used, direct smear testing and direct processing of specimens for the Xpert MTB/RIF assay may both be carried out on an open bench in an adequately ventilated area.

Disinfectants are equally available for use in the laboartory. They must be used for their rightful purpose.

Select disinfectants that are effective against mycobacteria based on the material to be disinfected.

PHENOL 2-5% in deionized water is highly irritating, and caution must be used in preparation. It is preferable to use phenolic derivatives:

Decontaminate equipment, surfaces and items or liquids before disposal (wear gloves)

Prepare the solution daily and leave in contact with the surface for at least 15 minutes to ensure decontamination.

CHLORINE (sodium hypochlorite, or bleach with 0.72% active chlorine) is an irritant, and is corrosive to metals and plastics: It is a general purpose disinfectant; also can be used to soak contaminated items. Allow at least 15 minutes to ensure decontamination. Prepare daily and store in a well-ventilated area (toxic gas). Do not autoclave.

ALCOHOL 70% leaves no residue but is volatile and flammable (keep far from open flames): Use as a disinfectant on skin (follow by washing with soap) and work surfaces (including metals).

PERACETIC ACID leaves no residue, but is stable for only 48 hours after preparation: Rapid action against all microorganisms.

Further to this the laboratory must have Sops to use in line with the safety standard. There should be an IPC Committee to address the issues related to safe working environment.

Risk Assessment

A risk assessment is simply a careful examination of what in your work could cause harm to people. A risk assessment must consider:

1. The bacterial load of materials, and the viability of TB bacilli
2. The route of transmission of TB
3. Whether the materials handled and the manipulations required for each procedure are likely to generate infectious aerosols
4. The number of manoeuvres in each technique that may generate aerosols
5. The workload of the laboratory and of individual staff members
6. The location of the laboratory
7. The epidemiology of the disease and the patient population
8. The level of experience and competence of lab staff
9. The health of lab staff (especially HIV-positive staff)

Steps in conducting Risk Assessment

- Identify potential hazards.
- Decide who might be harmed and how.
- Evaluate the risks and decide on precautions:
  - Determine the suitability of the physical space
  - Evaluate the staff's proficiency in following safe practices
  - Evaluate the integrity of safety equipment
- Record your findings and implement any necessary changes.
- Review your assessment and update it when necessary.
- A risk-assessment tool is available at ***http://www.gliquality.org***

CHAPTER 6

TB INFECTION PREVENTION AND CONTROL

Introduction

Tuberculosis infection prevention and control (IPC) is a critical component of End Tb strategy. It is a combination of measures aimed at minimizing the risk of TB transmission within populations. IPC requires and complements the implementation of core interventions in TB control, HIV control and strengthening of health systems.

Tuberculosis infection control is growing in importance because of the association of TB with HIV, the emergence of drug resistant TB (DR-TB) and increased risk of transmission among contacts of TB patients, in health care facilities and other congregate settings such as prisons and schools. These populations have been found to have a higher TB burden compared to the general population.

IPC Measures

There are three levels of TB infection control measures:

- Administrative (managerial) control measures
- Environmental control measures
- Personal protective equipment (respiratory protection).

Administrative control measures are the most important among the three levels. Environmental control measures and personal protective equipment (respiratory protection) will not work in the absence of solid administrative controls.

Each level operates at a different point in the TB infection control process:

- **1st priority**; Administrative control measures reduce HCW and patient exposure
- **2nd priority**; Environmental control measures reduce the concentration of infectious droplet nuclei
- **3rd priority**; Personal protective gear (respiratory protection) protects HCWs, patient and family members in areas where the concentration of droplet nuclei cannot be adequately reduced by administrative and environmental control measures.

1. Administrative Control Measures

These are defined as the managerial or work practices that reduce the risk of TB transmission by preventing the generation of droplet nuclei and limiting exposure to droplet nuclei.
There are four key components to good work practice (and administrative) controls. These include:

a. TB Infection, prevention and Control Assessment
b. Development of an infection control plan
c. Patient management
d. Infrastructure management i.e. clinics, laboratory and pharmacy.

a) TB Infection, prevention and Control Assessment

At facility and community levels, the Tuberculosis Infection prevention and Control assessment entails an initial and ongoing evaluation of the risk of TB transmission.

The Infection Control assessment should cover the following topics:

- Review of the statistical reports on TB in the community and facility
- Identification of the most-at-risk settings within the facility and prioritize them for initial efforts to improve TB infection control
- Identification of categories of HCWs that need to be included in a TB Screening program
- Identification of mechanisms to prompt recognition and reporting of presumptive TB episodes of transmission in the facility and community.

b) TB Infection, prevention and Control Plan

All relevant stakeholders should be involved in the development and review of the TB IPC plan.

This Plan should be implemented and monitored according to its recommendations.

The Plan should include:

- Description of the incidence or TB and TB/HIV in the facility
- Assessment of HCW training needs and training plan
- Administrative policies with regard to triage and screening, referral and diagnosis, separation and isolation
- Using and maintaining environmental controls
- Policy on the training and use of respiratory protection
- Area-specific infection control recommendations
- Description of roles and responsibilities for implementation and monitoring the infection control plan
- Time-line and budget A sample of TB infection, prevention and control plan template (Annex)

c) Patient Management

Table 6.1: Seven Steps for Patient Management to prevent transmission of TB in Community and health care settings

Step	Action	Description
1.	**Screen**	• Early identification of TB suspects or confirmed TB patients. This can be achieved by assigning a health worker to screen patients for prolonged cough immediately they arrive at the facility.
2.	**Educate**	• Instruct all patients with chronic cough on cough hygiene i.e. covering the nose and mouth when coughing or sneezing, - Where possible provide face masks or tissues to assist them in covering their mouths. • Educate on safe sputum disposal methods
3.	**Separate**	TB suspects and patients must be separated from other patients in a well-ventilated waiting area
4.	**Investigate for TB or Refer**	TB **diagnostic tests** should be done **onsite or**, if not available onsite, the facility should have an established link with a TB diagnostic and treatment site to which symptomatic patients can be **referred.**
6.	**Treatment**	• Confirm the diagnosis of TB disease within 2 hours for sputum smear microscopy and genexpert results and 2-6 weeks for culture. • Patients diagnosed with TB should be immediately started on anti-TB treatment on the same day
7.	**Discharge Plan**	For inpatient and outpatient settings, coordinate a discharge plan with the patient for continuity of care

2. Environmental Control Measures

These are measures that are used to **reduce the concentration of droplet nuclei in the air**. Such measures include maximizing natural ventilation and controlling the direction of airflow. In Kenya, opening windows and doors is the most practiced form of environmental control especially in resource limited settings.

There are two types of environmental controls:-

1. Natural ventilation

Simple natural ventilation may be optimized by maximizing the size of the opening of windows and doors and locating them on opposing walls.
**Where possible, the use of natural ventilation should be maximized before considering other ventilation systems.*

2. Mechanical ventilation

Well-designed, maintained and operated fans (mixed-mode ventilation) can help to obtain adequate dilution when natural ventilation alone cannot provide sufficient ventilation rates. In some settings, mechanical ventilation (with or without climate control) will be needed. This may be the case, for example, where natural or mixed-mode ventilation systems cannot be implemented effectively, or where such systems are inadequate given local conditions (e.g. building structure, climate, regulations, culture, cost and outdoor air quality).

The following are the five main principles of environmental control measures

- Facility design
- Dilution (e.g. Ventilation systems)
- Filtration (e.g. HEPA filters)
- Purification (e.g. UVGI Systems)
- Disinfection (e.g. chemical, thermal)

Facility Design

The design should take into consideration

1. Patient flow pattern
    - Minimizes congregate situations
    - Provide areas for segregation of potentially infectious patients
    - Provide isolation rooms for infectious patients
    - Minimize cross infection

2. Maximize natural ventilation
    - Direction of wind flow
    - Placement and sizes of doors, windows and corridors
    - Maximize natural draught through chimney affects, ventilation grills, open verandas
    - Promotes air-flow patterns from the least infected (health care worker) to the most infected (patients)

3. Maximize availability of sunlight as a natural deterrent to growth of MTB colonies

Dilution

This is the simplest, extremely effective, and least expensive technique

It involves removal and dilution of infectious air by maximizing natural ventilation

Filtration

It's a method that involves removing infectious particles and brings back filtered air. This involves use of HEPA cleaner (High Efficiency Particulate Air cleaner).

- In-duct application
- In conjunction with Room air cleaner (mobile or fixed)

Purification

It involves use of Ultra Violet Germicidal Irradiation (UVGI) to inactivate M. tuberculosis organisms

Disinfection

- Chemical disinfection for general equipment and laboratory services.
- Thermal e.g. steam sterilization, autoclaving

In the face of inadequate or insufficient administrative control measures, environmental control measures will not eliminate the risk.

3. Personal protective equipment PPE (respiratory protection)

This refers to items specifically used to protect the health care provider, the patient and the community from exposure to body substances or from droplet or airborne organisms. Personal protective equipment includes gloves, aprons, gowns, caps, surgical masks, respirators and protective eye wares.

Table 6.2: Type of Recommended Protective Equipment and Recommended Use

Type of PPE	Recommended use	Primary protects
Gloves	• When there is a reasonable chance of hands coming in contact with blood or other body fluids, mucous membranes, or non- intact skin • Before performing invasive medical procedures, for example, when inserting vascular devices such as peripheral venous lines • Before handling contaminated waste items or touching contaminated surfaces	Service providers
Caps, gowns or aprons	• When performing invasive procedures during which tissue beneath the skin is exposed • When handling immunocompromised patients or • When handling patients with infectious disease • When handling contaminated was	Service providers, patients
N-95 masks	• When handling patients with airborne or droplet infections	Service providers, visitors and care givers
Surgical/ Procedural masks	• When performing invasive procedures • When handling medical waste • When handling medical waste	patients, laboratory staff

Goggles or glasses	• Situations in which splashing of blood, body fluids, secretions, or excretions are likely	Service providers, and laboratory staff
Closed boots or shoes	• Situations in which sharp instruments or in which spillage or infectious agents are likely • When handling immunocompromised patients In the nursery	Service providers and patients

Use of surgical or procedure masks for patients

- Surgical masks are used by the patients to prevent transmission of droplets during exhalation - coughing, sneezing, talking or singing.
- However, it is still paramount to educate the patient on cough etiquette practices such as covering mouth using tissues or clothes, not spitting on floor and proper disposal of soiled tissues.
- Patient and HCW education regarding the importance and appropriate use of wearing surgical masks should accompany their distribution.

N 95 for health care workers

N 95 are a special type of respirators that provide 94-95% filtration efficiency against 0.3-0.4 micrometer particles. They should be closely fitted to the face to prevent leakage around the edges. If the respirator is not worn correctly, infectious droplet nuclei can easily enter a person's airways, potentially resulting in infection.

Wearing and fitting a respirator properly

- The N95 masks can be re-used repeatedly for several weeks if they are properly stored before disposal.
- Respirators should be stored in a clean dry location devoid of humidity, dirt and filter damage.
- Plastic bags should never be used since they retain humidity.

It is important to remember that a surgical mask worn by HCWs may not adequately protect them from inhalation of air contaminated with M. tuberculosis. Respirators are the preferred device to reduce the concentration of M. tuberculosis bacilli inhaled.

Protection in high risk areas

- Respirators should be worn by all personnel entering high risk areas such as bronchoscopy rooms, sputum induction rooms, MDR-TB isolation wards, people handling specimens in the laboratory, MDR-TB Clinic.
- The use of powered air- purifying respirator (PAPR) is also recommended where high risk procedures are performed, for they are cost-effective and are re-usable and does not require fit testing.

TB Laboratory Safety

Laboratory safety

The most important factor in the prevention of laboratory TB acquired infection is good technique on the part of the individual health care provider. Specialized equipment may aid good laboratory practice but does NOT replace it. Proper PPE should be worn in the laboratory while processing samples this is in regard to respirators, laboratory coats, gloves.

Multi-Drug Resistant and Extensively Drug Resistant TB

The health care workers working with DR TB patients should take necessary preventive precautions.

- The community should be well educated about TB infection, prevention and control.
- DR-TB care providers at community level should be sensitized on risk of transmission and be provided with basic protective equipment.
- DR-TB patients should be provided with basic personal protective equipment for use in the home setting where vulnerable groups like children under five, elderly and chronic ill people.
- In the event that a DR TB patient is a nursing mother to an infant, timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby.
- She should not be completely separated but care of the infant should be left to family members until she becomes sputum smear negative, if this is feasible.
- When the mother and infant are together, this common time should be spent in well-ventilated areas or outdoors. The mother should use a surgical mask until she becomes sputum smear negative.

Infection Control Measures in Special Settings

There are special settings in the community that are at a higher risk and call for special attention as far as TB infection, prevention and control is concerned.
These include:-

I. Congregate settings

- Prisons and remand cells
- Informal settlements (slums)
- Refugee and internally displaced persons (IDP) camps
- learning institutions (schools, colleges,
- Security forces training camps (military, GSU, police national youth service etc)

Prisons and remand cells

- The prison and remand cells should follow and implement TB infection control guidelines.
- All inmates should be screened for TB using the MOH PF 10 tool at admission and subsequently, after every 6 months.
- Active advocacy and sensitization of relevant ministry and departments for the implementation of TB infection control in the prisons should be done.

Informal settlements (slums)

- To reduce the transmission of Tuberculosis in the informal settlement, adequate sensitization and advocacy on adequate ventilation on the existing structures/ housing.
- Sensitization on community TB infection control should be emphasized and early health seeking practices be encouraged among community members.
- Active Tuberculosis screening and contact and defaulter tracing should be conducted in the community.

Refugee and internally displaced persons (IDP) camps

- Tuberculosis screening of refugees at cross border points and camp should done upon arrival.
- Symptomatic patients should be tested for Tuberculosis using gene xpert and sent for culture and Drug Susceptibility Test to rule out Drug resistant Tuberculosis.
- Cross border transfer of refugees with Tuberculosis should be done through the Learning institutions and security forces training camps

Tuberculosis infection prevention and control should be incorporated in the school health program and training camps.

II. Public services transport

- Matatus, buses and trains
- Air transport

- Advocacy and sensitization of relevant ministries and other stakeholders on infection prevention and control of Tuberculosis is key.

- Public Transport users should ensure adequate ventilation by opening all the windows or applying mechanized ventilation.
- Transfer of TB patients from one facility to another should be by well ventilated means of transport with personal respiratory protective devices.
- Patients known to have potentially infectious Tuberculosis should be advised not to travel on commercial aircraft until there is no longer a risk of transmitting infections to others.

Infection Control and Legal Implication

TB, MDR-TB patient, and the community should be adequately educated on the importance of adhering to DOTs and DOTs Plus strategy. Patients who may refuse to adhere to the treatment will have to be managed according to the existing laws and guidelines.

References

1. *Tuberculosis Infection Control in the Era of Expanding HIV Care and Treatment, CDC-WHO, 2006*
2. *Guidelines for the Prevention of Tuberculosis in Health Care Facilities in Resource-Limited Settings, WHO, 1999*

CHAPTER 7

NUTRITION ASSESSMENT COUNSELLING AND SUPPORT

Objectives of Nutrition in Tuberculosis, Leprosy and Lung Disease

1. To prevent and correct malnutrition
2. Reduce the effects of medication on patients
3. To improve and maintain the nutritional status of patients
4. Promote adherence
5. To promote drug efficacy
6. Restoring fat-free mass in chronic obstructive pulmonary disease.

Definitions

Nutrition

Refers to the sum of all processes involved in taking in of nutrients and their assimilation and use for proper body functioning and maintenance of health. The successive stages include; ingestion, digestion, absorption, assimilation and excretion.

Nutrients

These are chemical substances obtained from food and used in the body to provide energy, structural materials and regulating agents to support growth, maintenance and repair of the body's tissues. Nutrients are categorized into two; macronutrients and micronutrients

Macronutrients

This refers to a nutrient that is required in large amounts for the normal growth and development.

Protein, fat and carbohydrates are macronutrients that make up the bulk of a diet and supply the body's energy.

Micronutrients

This refers to essential dietary elements that are needed only in very small quantities for normal body function. Micronutrients are divided into two classes as Type I, which includes iodine, iron, Vitamins A and C. Type II include; magnesium, sulphur, nitrogen, essential amino-acids, phosphorus, zinc, potassium, sodium and chloride.

Malnutrition

Malnutrition is defined as "a state in which the physical function of an individual is impaired to the point where he/she can no longer maintain adequate bodily performance processes such as growth, pregnancy, lactation, physical work, and resisting and recovering from disease."

It is also a general term that refers to either over nutrition or under nutrition or both. It may result from an unbalanced, insufficient or excessive dietary intake or from impaired absorption, assimilation or use of nutrients. There are various forms of malnutrition.

Over nutrition

Is a condition of excess nutrient and energy intake over time, it may lead to morbid obesity which is an abnormal accumulation of body fat, usually 20% or more above an individual's ideal body weight

Under nutrition

This refers to a state when the nutritional status of the person is sub-optimal and thereby health and growth may be limited. It may be due to illness that impair nutrient intake and metabolism or result from inadequate intake of macronutrients, micronutrients or both.

Micronutrient deficiencies

This is a form of malnutrition often referred to as hidden hunger. It is caused by inadequate intake of vitamins, minerals and trace elements.

Composition of Food

Table 7.1: Different foods provide various nutrients that have different functions in the body

Nutrient	Function	Food sources
Protein	- body-building - Aiding in immune function Controlling foods biochemical reactions	Animal foods: Meat, fish, milk & dairy products, eggs Plant foods: Legumes (beans, lentils),nuts (groundnuts, peanuts) , soybean products (meat, bean, milk)
Carbohydrates	- Source of energy	Cereal grains and their products: maize, millet, wheat, sorghum, rice, Roots and Tubers: Potatoes, cassava, yam, sweet potatoes, plantain (cooking bananas)
Lipids (Fats/oils)	- Energy reserve - Protection of vital organs - Thermal insulation	Visible fats (solid at room temperature) Visible oils (liquids at room temperatures) Invisible fats/oils: nuts, animal foods, avocado
Vitamins	- Reducing infection by supporting in the immune system -Aiding in metabolism	Fruits: mango, oranges, pawpaw, pineapple, passion, melon Vegetables: sukuma wiki, cabbages, spinach, lettuce, carrots, broccoli

Minerals	- responsible for building structures like bones and teeth - Support various chemical reactions	vegetables, meats and meat products, milk and milk products
Fibre	-Regulate digestion -Reduction of cholesterol levels (soluble fibre)	Soluble: Legumes, apples, carrots, beans, cucumber, oranges Insoluble: Whole grains, fruits, vegetables
Water	-Transportation of nutrients -Transportation of waste material -Normal body functioning	Drinking water, Juices, soups

Components of a Healthy Diet

When planning a meal, it is important to consider the following basic principles. The food guide pyramid below will help you explain how to achieve good feeding practices.

Figure 7.1: Food Pyramid

Source: *Diabetes Educator, 2010*

Table 7.2: Food Pyramid Guide

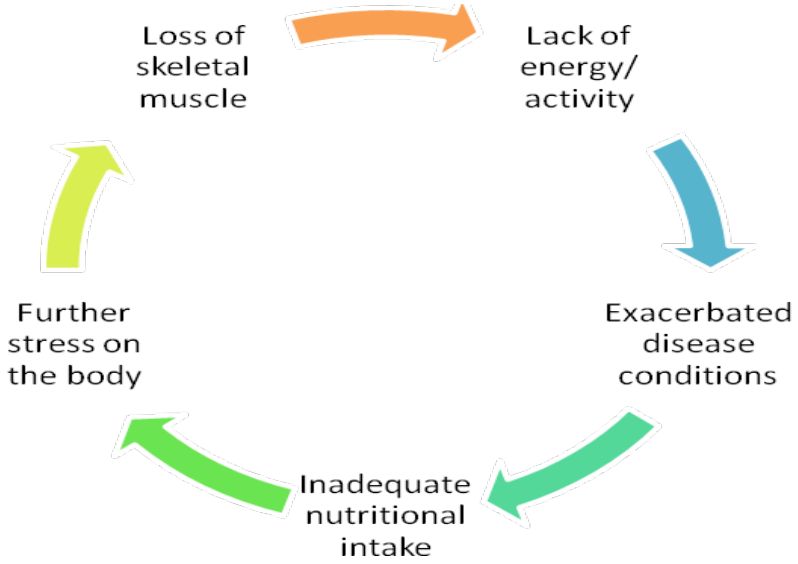
Food group	Recommended number of servings per day	One serving size is equal to either:- (1 cup = 250mls)
Grains , bread and other starches	6 -11	1 slice of bread or ½ cup of cooked rice/cereals or ¼ cup dry cereals or ½ cup pasta or 1 boiled/roasted green banana or A fist size of root tubers (arrow roots ,sweet potatoes, yams, cassava) or ½ cup boiled mashed Irish potatoes
Vegetables	3 – 5	½ cup vegetables cooked Or 1cup vegetables raw
Fruits	2 – 4	1 cup fruit juice Or 1 medium piece fresh fruit
Milk and milk products	2 – 3	1 cup skimmed/low milk Or 3/4 cup yoghurt
Meat and meat substitutes	2 – 3	57 – 87 cooked lean meat, Or poultry 28gms, or 1 egg, or cheese 28.5 gms,1/2 fish
Fats and oils	Use sparingly	1 tea spoon margarine, or salad dressing, or peanut butter 1 table spoon
For further information/clarification, consult a nutritionist/dietician		

Relationship Between Nutrition Lung Diseases and Leprosy

Pulmonary diseases with nutrition implications include TB, COPD, Asthma, Pneumonia, bronchitis, among others. Poor nutrition status in lung disease has been related to adverse effects that may contribute to complications and increased mortality. Patients with low body weight have greater gas trapping, lower diffusing capacity and less exercise capacity. The presence of malnutrition and weight loss is associated with poor prognosis

In lung disease, resting energy expenditure (REE) is 15-20% above the normal values for adults and 25-50% for infants. The increased energy required for breathing accounts for the difference.

Figure 7.2: Relationship between nutrition lung diseases and leprosy

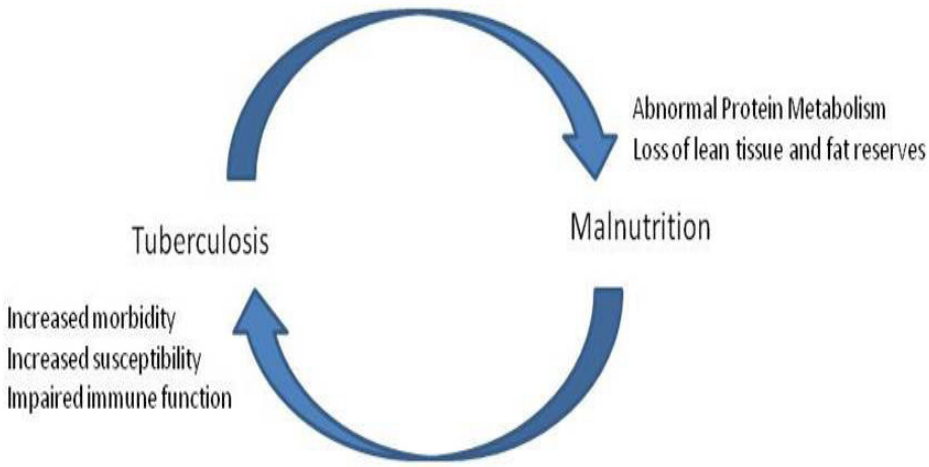


TB and Malnutrition

TB affects the metabolism of important nutrients such as protein and some micronutrients. Malnutrition on the other hand limits cell mediated immunity and increases susceptibility to infection. Nutritional deficiencies are associated with impaired immune functions; This affects cell mediated immunity by reducing the expression of gamma interferon, tumor necrosis alpha and other myco-bactericidal substances that are important for containing and restricting TB. This leads to nutritional stress and weight loss, thus weakening immune system causing body's inability to fight infections.

Nutritional status is one of the most important determinants of resistance to infection. It is well known that there is a close association between TB and malnutrition as malnutrition increases the risk of developing TB and the vice versa

Figure 7.3: TB and Malnutrition



Source: *TB Nutrition guidelines, 2012*

Malnutrition markedly increases mortality among both TB and HIV/AIDS patients and should be treated concurrently with treatment of the infections.

Active TB often leads to malnutrition. TB patients frequently suffer from a loss of weight and appetite and consequently present a low body mass index and skin fold thickness. Nutritional derangements include;

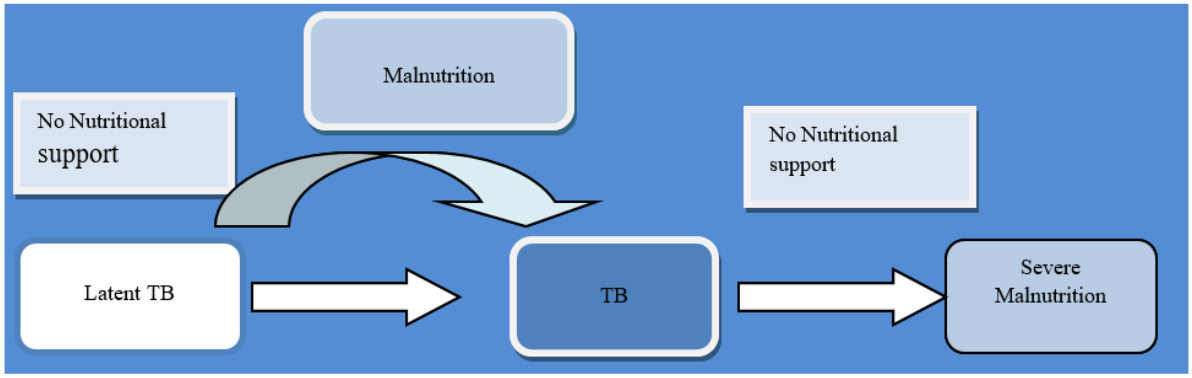
- There's a 13% increase in basal metabolic rate (BMR) change with every 1 degree Celsius rise in body temperature
- The adipose and glycogen stores normally decrease due to increase in energy expenditure.
- Loss of body fluids - sweating and urination during the acute phase hence electrolyte loss.
- Loss of body weight due to increased catabolism
- Reduced appetite and ability to take food (anorexia, Cachexia and generalized weakness).
- Reduced ability of body to absorb nutrients
- Increased nutritional needs through metabolic changes
- Micronutrient deficiencies like Zinc, Vitamins A, C and D and Iron

Consequences of malnutrition

- Reduced access to food due to morbidity/low productivity
- Less activity, less lung function and less heart function
- Serum protein levels can affect airway function and diffusing capacity of lungs
- Cachexia also affects lung function
- Decreased cough and inability to mobilize secretions

- High likelihood of progression from latent infection to active disease when malnourished or weakened immune system (diminished functions of T-lymphocytes and phagocytic cells)
- Increased risk of mortality
- Diminished pharmacal-dynamic effectiveness of anti-mycobacterium drug regimen
- Impair the protective efficacy of Bacillus Calmette-Guerin (BCG)
- Progressed disabilities
- Delayed and prolonged wound healing

Figure 7.4: Consequences of malnutrition



Role of nutrition

Optimal Nutrition combined with medical treatment is an important component in treatment and care. Good nutrition enhances:

- Growth, development, replacement and repair of cells and tissues.
- Helps chemical processes such as digestion, metabolism, assimilation and excretion
- Restores and protects the integrity of the immune system.
- Prevent wasting and other forms of malnutrition micronutrient included.
- Delay HIV progression.
- Improve drug efficacy
- Optimize cellular activity and tissue/organ function by providing sufficient amounts that meets daily body requirement

Nutrition Assessment Counselling and Support

Nutrition assessment counseling and support (NACS) aims to establish routine nutrition assessment as an integral component of facility- and community-based health care providers to deliver nutrition-specific services. It links clients to nutrition-sensitive interventions provided by the health, agriculture, food security, social protection, education and rural development sectors.

Nutrition assessment can;

- Identify medical complications that affect nutritional status
- Track growth and weight trends
- Detect diet habits that make it difficult to improve health or that increase the risk of disease
- Inform nutrition messages and counseling
- Establish a framework for an individual nutrition care plan, which specifies nutrition goals and interventions, feasible changes in behavior, and practices to meet those goals

Types of Nutrition Assessment

a) **Anthropometry**

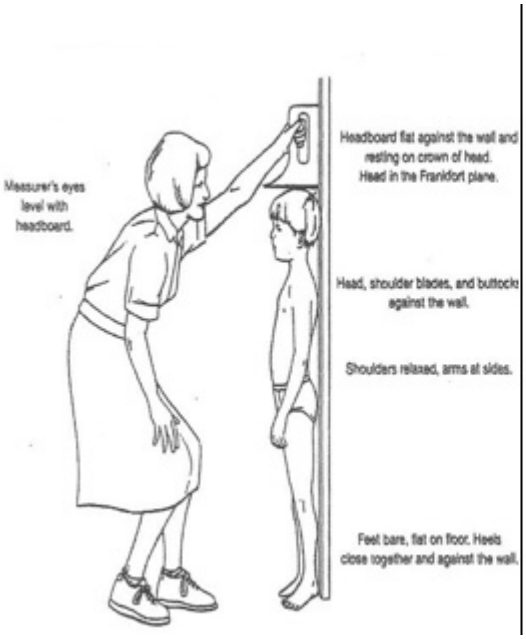
Anthropometric screening is carried out through serial measurements of weight, height, mid upper arm circumference (MUAC) and skin fold thickness (SFT). The values obtained are used to show changes in body mass and dimensions as follows:

Taking weight

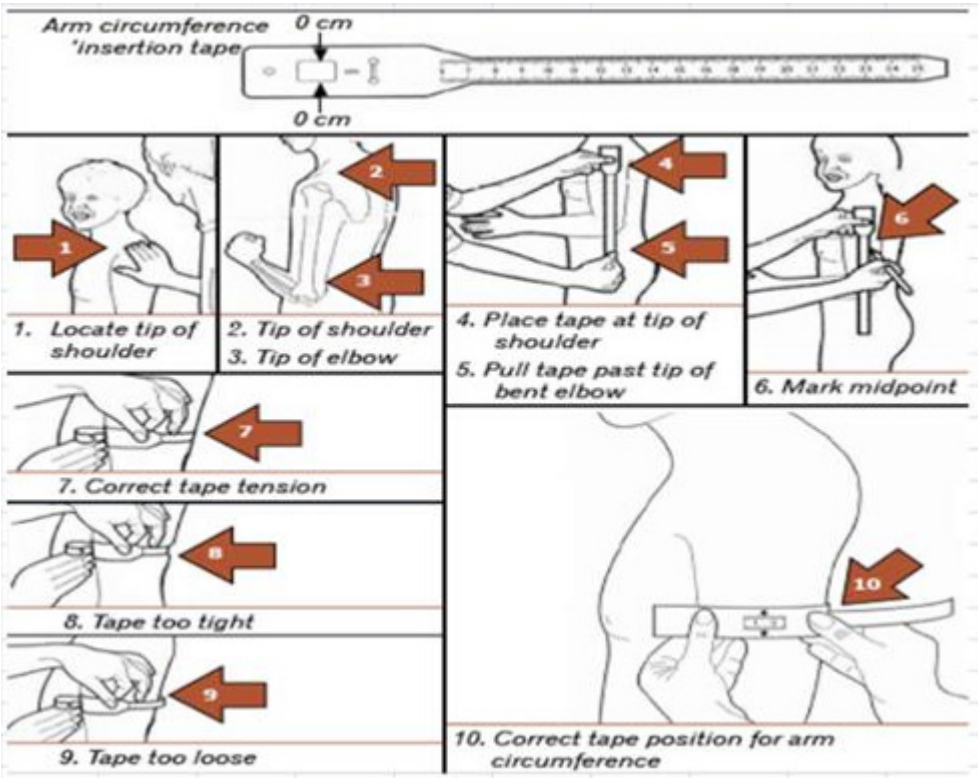
- Weight should be taken using a functional medical scale which should be calibrated before starting. If a UNI scale, standardize with a known weight after 100 weights.
- Place the scale on a flat even surface
- Zero the weighing scale (i.e. make sure the arrow is on 0)
- Ensure that the weighing scale is at eye level
- Before taking weight ensure client is on light clothing or the child, take all his/her clothes off

All patients should have their weight taken and recorded immediately

Taking height



Taking Mid Upper Arm Circumference



b) Biochemical

These are chemical assays/ Lab assessments/analysis in most cases done on body fluids and have nutrition implications e.g Haemoglobin ,sugar levels, Liver function , CD4,Thyroid function, calcium levels, creatinine, kidney functions.

Table 7.3: Normal Biochemical Values for Male and Female

COMPONENT	GENDER	VALUE
Haemoglobin	Male: Female:	13-18g/dl. 11.5-16.5g/dl.
Sodium	Male & Female	135-145mmol/litre.
Potassium	Male & Female	3.5-5.0mmol/litre.
Chloride	"	96-106mmol/litre.
Ammonium	Male: Female:	34-58mmol/litre. 17-51mmol/litre.
Urea	Male & Female	2.5-7.0mmol/litre.
Creatinine	"	60-130mmol/litre.
Total calcium	"	2.12-2.62mmol/litre.
Albumin	"	35-50g/litre.

Globulin	"	20-40g/litre.
Calcium	"	2.2-2.64mmol/litre or 8.8-10.6mg/100nl.

COMPONENT	GENDER	VALUE
Cholesterol	Male & female	3.2-8.5mmol/litre or 120-330mg/100ml
Glucose [fasting]	"	3.3-5.9mmol/litre or 60-108mg/100ml.
Urinary values [24 hr urinary excretion]		
Protein	"	Up to 00 g/24hrs.
Albumin	"	Up to 25mg/24hrs.
Ketones	"	0.1-0.3mmol or 5-15mg/24hrs.
Calcium	"	2.5-7.5mmol/24hrs.
Normal values in liver functions tests		
COMPONENT	**GENDER**	**VALUE**
Total Serum Bilirubin		5-17 mmol/litre
Bilirubin esters	"	<6mmol/litre
Urine Bilirubin	"	Negative result
Serum albumin	"	35-50g/litre
Serum alkaline phosphate	"	30-110IU/litre
Serum alanine amino transferase	"	5-40IU/litre
Serum aspartate amino transferase	"	5-40IU/litre

c) Clinical assessment;

This involves physical observation/ judgement Signs of nutrient deficiencies like visible wasting, hair changes, oedema, skin changes

Table 7.4: Clinical Assesment for Nutrition Deficiencies

Body part or system	Signs/Symptoms	Possible deficiency
Hair	Lackluster, Thinness, sparseness, dryness, dyspigentation, easy pluckability, texture change	Proteins, protein-energy, Zinc, copper biotin.
Face	Paleness, Moon face (swollen), Greasy scaling around nostrils (nasolabial)	Riboflavin, Niacin, Pyridoxine, Iron
Eyes	Pale white eyes and eyelid lining (pale conjunctivae), Redness and fissuring of eyelid corners dullness and dryness (corneal or conjunctival xerosis), redness, lesions of conjunctivae (Bitot's spots)	Iron, folate, vitamin A, C, B2 B_6 and B_{12}
Mouth	Angular redness, lesions or scars at the corners of the mouth (stomatitis), swelling and redness of lips and mouth (cheilosis)	Riboflavin Niacin pyridoxine iron
Tongue	Smoothness, slickness (filiform papillary atrophy), beefiness, redness, pain (glossitis), swollen, magenta color	Niacin, pyridoxine, riboflavin, vitamin B_{12} folate, iron
Gums	Swelling, sponginess, bleeding, receding	Vitamin C
Skin	Dryness, scaling, lightening of skin color often centrally on the face (diffuse pigentation), rough, gooseflesh skin (follicular hyperkeratosis), small skin hemorrhages (petechiae), excessive bruising, hyper pigented patches that may peel off, leaving superficial ulcers or hypo pigented skin (flaky paint dermatosis), oedema, delayed wound healing.	Vitamin A, C and K, Zinc, essential fatty acids, protein, Niacin.
Nails	Spoon-shape (kiolonychia), pale, brittle, ridged.	Iron
Glands	Enlarged thyroid or parotid	Protein, iodine
Musculoskeletal system	Bowlegs knock knees, enlarged joints, hemorrhages, muscle and fat wasting.	Protein-energy, Vitamin D and C, Calcium
Neurological system	Mental confusion, irritability, psychomotor changes, motor weakness, sensory loss	Thiamin, Riboflavin and Vitamin B12

d) Dietary assessment

24 hour recall, food diary, food frequency and diet history

e) Economic and social status

Includes the assessment of food security, source of income, number of household members and social support

f) Functional

Functionality of body parts assess the energy levels- (ability to prepare or consume meals and mobility) lethargy and disability.

Making a Nutrition Diagnosis

This is the identification of an existing nutrition problem which may be acute or chronic in nature and varies as the patient/client/group's response changes.

A health worker should;

1. Look out for the signs and symptoms
2. Be able to identify the nutrition problem based on the assessment and classification of nutritional status
3. Probe to find out the etiology of the problem

At the nutrition diagnosis step documentation required includes;

Anthropometric cut off points(Z score/BMI/AGE /classification of malnutrition)

Changes can be expressed as a percentage of weight loss or gain;

Rapid weight loss is associated with hospitalization risks	5% of usual body weight over a 2 to 3 month period warrants a carefully executed diagnostic evaluation to determine any correctable or treatable confounding conditions.
Associated with Mortality	More than a 10% decrease in body weight over 2 to 3 requires follow up

Nutrition Diagnosis

Nutrition Diagnosis is the second step of the Nutrition Care Process, and is the identification and labeling that describes an actual occurrence, risk of, or potential for developing a nutritional problem that dietetics professionals are responsible for treating independently. At the end of the assessment step, data are clustered, analyzed, and synthesized. This will

reveal a nutrition diagnostic category from which to formulate a specific nutrition diagnostic statement. A nutrition diagnosis changes as the patient/client/group's response changes.

Nutrition Diagnosis Components

Nutrition Diagnosis has 3 distinct components:

i. Problem (P) (Diagnostic Label)

ii. Etiology (E) – this is the cause and/or Contributing Risk Factor(s)

iii. Signs/Symptoms (S) – these are the Defining Characteristics

Nutrition Diagnostic Statement

A nutrition diagnostic statement is written in a PES format that states the Problem (P), the Etiology (E), and the Signs & Symptoms (S). However, if the problem is either a risk (potential) or wellness problem, the nutrition diagnostic statement may have only two elements, Problem (P), and the Etiology (E), since Signs & Symptoms (S) will not yet be exhibited in the patient.

Table 7.5: Assessment Diagnosis and Classification of Malnutrition

ASSESS				
HISTORY	**LOOK AND FEEL**	**CRITERIA**	**CLASSIFICATION**	**TREATMENT/CARE**
Ask client or refer to records: 1. Has the client lost weight in the past month/since the last visit? 2. Has the client had: – Active TB (on treatment)? – Another chronic OI or malignancy (e.g., oesophageal infections)? – Mouth sores/oral thrush? 3. Has the client's body composition/fat distribution changed noticeably? – Thinning of limbs and face? – Fat distribution on limbs, breasts, stomach, back? 4. Has the client had: – Nausea and vomiting? – Persistent fatigue? – Poor appetite?	1. If client has oedema on both legs or base of the spine, rule out pre-eclampsia, kidney problems, elephantiasis, heart failure, and wet beriberi (vitamin B1 deficiency with oedema) 2. Measure client's weight (kg) and height (cm) 3. Compute BMI $\frac{\text{Weight (kg)}}{\text{Height (m}^2\text{)}}$ 4. Measure MUAC for pregnant women, women up to 6 months post-partum, and adults who cannot stand straight 5. Examine for conditions that cause secondary malnutrition 6. Look for complications and danger signs (anaemia, severe dehydration, active TB, severe bilateral oedema)	**Adults (non-pregnant and non-post-partum)** BMI: < 16 If can't measure BMI, MUAC: < 19 cm **OR** Bilateral pitting oedema (both feet or legs are swollen, and the skin remains indented when pressed with a finger) **Pregnant women and women up to 6 months post-partum** MUAC: < 21 cm or < 23 cm with weight loss	**SAM with complications** (fever, hypothermia, severe anaemia or dehydration, vomiting, bilateral oedema +++) **or** no appetite	**Inpatient treatment** Follow Nutrition Care Plan for SAM in Inpatient care
			SAM with appetite and no complications BMI: < 16 **or** MUAC: < 19 cm and no danger signs	**Outpatient treatment** Follow Nutrition Care Plan for SAM in Outpatient Care
		Adults (non-pregnant and non-post-partum) BMI: ≥ 16.0 to < 18.5 MUAC: ≥ 19.0 to < 21.0 cm **Pregnant women and women up to 6 months post-partum** Poor weight gain MUAC: ≥ 21 to < 23 cm	**Moderate/mild malnutrition** **Significant weight loss**	**Follow Nutrition Care Plan for MAM**
		Adults (non-pregnant and non-post-partum) BMI: ≥ 18.5 to 24.9 MUAC: ≥ 21.0 cm **Pregnant and post-partum women (up to 6 months)** MUAC: ≥ 23 cm	**Normal**	**Follow Nutrition Care Plan for Normal Nutritional Status**

Table 7.6: Assessment Diagnosis and Classification of Malnutrition in Children

ASSESS				
ASK	LOOK AND FEEL	CRITERIA	CLASSIFICATION	TREATMENT/CARE
Ask mother or caregiver or refer to records: 1. Has the child lost weight in the past month/since the last visit? 2. Has the child had: a. A cough for more than 21 days? (This may be a result of HIV-related chronic lung disease, such as lymphocytic interstitial pneumonia or bronchiectasis) b. Active TB (on treatment)? c. Diarrhoea (three or more stools per days)? d. Another chronic OI or malignancy?	**1. Look for severe visible wasting:** – Loss of muscle bulk on arms, shoulders, buttocks, and thighs, with visible rib outlines – Sagging skin on buttocks **2. Check for oedema** (swelling) in both feet **3. Weigh the child** **4. Measure MUAC** **5. If MUAC measurement is not possible, then measure weight-for-age and look at the shape of the curve on the growth chart** – Has the child lost weight since the last visit? (Measure again to confirm current weight) – Is the growth curve flattening? – Is the child gaining weight?	**Bilateral pitting oedema** (both feet and/or legs are swollen, and the skin remains indented when pressed with the thumb) **OR** MUAC: 6–59 months: < 11.5 cm 5–9 years: < 13.5 cm 10–14 years: < 16.0 cm 15–17 years: < 17.5 cm **AND** Appetite test (pass or fail)	**SAM** **Bilateral oedema +++, marasmic kwashiorkor** **With no appetite or with medical complication** (anorexia, intractable vomiting, convulsions, no alertness, lethargy, lower respiratory tract infection, high fever, severe anaemia or dehydration, hypoglycaemia, hypothermia) **With appetite and without medical complication** Clinical wellness Alertness Caregiver able/willing to manage SAM at home and return to clinic every 14 days	**Inpatient treatment** **Follow Nutrition Care Plan for SAM in Inpatient Care** **Outpatient treatment** **Follow Nutrition Care Plan for SAM in Outpatient Care**
		MUAC: 6–59 months: ≥ 11.5 to < 12.5 cm 5–9 years: ≥ 13.5 to < 14.5 cm 10–14 years: ≥ 16.0 to < 18.5 cm 15–17 years: ≥17.5 to < 19.5 cm	**MAM** **Poor weight gain**	**Follow Nutrition Care Plan for MAM**
		Weight gain parallel to or higher than median growth curve MUAC: 6–59 months: ≥ 12.5 cm 5–9 years: ≥ 14.5 cm 10–14 years: ≥ 18.5 cm 15–17 years: ≥`19.5 cm	**Normal** **Growing appropriately**	**Follow Nutrition Care Plan for Normal Nutritional Status**

Nutrition Interventions

This describes activities to be carried out once malnutrition is identified where the nutritionist or nutrition service provider;

- Selects the suitable intervention for the patient
- Plans with the patient on how to implement it
- Implementing appropriate actions to meet /client/groups' nutrition needs.

Note;
The selection of nutrition interventions is driven by the nutrition diagnosis and provides the basis upon which outcomes are measured and evaluated.

Nutrition Counseling

Upon assessing the clients and making a nutrition diagnosis
This should be an interactive process where a nutrition service provider uses information from nutrition assessments to prioritize actions to improve nutritional status.

Nutrition education and counseling enlightens the patients on their status and requirements. Counseling helps identify client preferences, barriers to behavior change, and possible solutions to overcome those barriers. With this information, the client and care provider jointly plan a feasible course of action to support healthy practices. The care provider may use job

aids to select appropriate messages and guide counseling sessions. Group education on key nutrition topics can be provided in health facility waiting rooms or for community groups using various print and audiovisual media.

Table 7.7: Nutrition Interventions and Considerations

STEP 3: NUTRITION INTERVENTION • Purposely-planned actions designed with the intent of changing a nutrition-related behavior, risk factor, environmental condition OR aspect of health status • May target individual, a target group, or population at large. • Specific set of activities and associated materials used to address identified nutrition problem. • Directed at the etiology or effects of a diagnosis	
Intervention	What to consider
NUTRITION EDUCATION Provision of information and educational materials designed to improve health status, dietary habits and physical activity habits.	Critical nutrition points (CNPs) • *Assist the TB patient at nutritional risk in achieving a positive change in food habits.* • *Improve nutritional status and* • *Prevent nutrition related problems through optimal use of the supplemental foods and other nutritious foods.* • *Monthly assessments especially weight.* • *Increase food intake* • *Sanitation, food hygiene and water safety.* • *Positive living behaviors* • *Physical activity.* • *Drink safe, clean water 8 glasses a day.* • *Manage food drug interactions.* • *Provide micro nutrient supplement* • Follow-up and closely monitor the patient.
NUTRITION COUNSELING Should be patient-centered	Areas for counseling • *Weight management* • *Drug reaction* • *Adherence* • *Dual infection increase or reduce intake* • *Relapse* • *Referral from community* • *Rehabilitation*

FOOD AND/OR NUTRIENT DELIVERY
These are aimed at treating/correcting under-nutrition and preventing TB/HIV mortality risks. During active TB infection even well-fed patients have altered protein metabolism. A patient with active TB uses less protein to build up muscle, leading to increased oxidation of amino acids and increased oxidative stress that the body has to fight.
	• Food rations
	  • Take home rations, meals and snacks (3 meals and 3 snacks per day)
	• Supplementary foods
	  • Macronutrient food supplements
	  • Vitamin and mineral supplements
	  • Bioactive substance supplements
	• Therapeutic foods
	  • Medical food supplements
	  • Enteral / parenteral nutrition
	• Feeding assistance and feeding environment
	• Nutrition-related medication management

Nutrition Support

Nutrition support includes:

- Therapeutic and supplementary foods to treat moderate and severe under nutrition (wasting)
- Micronutrient supplements to prevent vitamin and mineral deficiencies
- Point-of-use water purification products to prevent water-borne disease

Vitamins and Minerals

The body should be provided with liberal amounts of the vitamins and minerals. In TB, conversion of beta carotene to retinol is affected in the intestinal mucosa (Decrease). The client should be supplemented with Vitamin A (every six months or as per the National Vitamin A supplementation schedule) and encouraged to eat vitamin A rich foods.

Patients on Isoniazid should ideally be supplemented with 10mg of pyridoxine B6 daily or 25mg once neuropathy is experienced since the drug inhibits its absorption. Additional amounts of vitamin C is recommended in the diet to facilitate healing of lesions.

Other antioxidants Vitamin E, zinc and selenium neutralize free radicals and prevent the production of peroxides from lipids.

Consider iron folic acid, supplementation depending on the haemoglobin level.

Water

Drink at least 8 glasses or more of safe water per day. This helps in preventing dehydration and flushing out toxins.

Fiber

Low fiber diet is recommended as the patient nutrient intake is impaired. High fiber is likely to keep the patient feeling full but on few calories.

General recommendations

- Diet should be based on locally available foods
- Maintain a balanced diet with diversity
- The cost of the advised food should be affordable not catastrophic to the house hold
- Foods should be rich in all the essential Nutrients, carbohydrates proteins vitamins and minerals
- The food should be appetizing and easy to ingest and digest
- Warm food often provides more appetite than cold food.
- Patients should eat enough food to maintain adequate nutrition.
- Avoid intoxicants and other harmful substances e.g. alcohol, cigarettes

Nutrition Management of TB in Pregnant and Lactating Women

A healthy well-nourished woman should gain between 10 kg and 14 kg during pregnancy, to increase the likelihood of delivering a full-term infant weighing at least 3.3 kg. To support increased nutrient needs during pregnancy and lactatigon, women are advised to consume additional amount of foods (WHO, TB, 2013). TB and HIV/AIDS could affect pregnancy outcome if the increased dietary needs are not met.

Weight gain Recommendations for Pregnancy

Pre pregnancy BMI	Weight in Kgs.
BMI < 19.8	12.5 – 18.0
BMI 19.8 – 26.0	11.5 – 16.0
BMI > 26.0 – 29.0	7.0 – 11-5

Source: *Food and Nutrition Board -1999*

Table 7.8: Recommended Energy and Protein Requirements for Women During Pregnancy and Lactation in TB

PREGNANCY				
	Energy requirements		Protein requirements	Extra energy for women with TB and or HIV
	Total nutrient requirements	36-40 kcal/ kg/day	0.8-1.0g/kg/day	20-30%
	First trimester0-12 wks	+150 kcal/day	+0.7g/kg	20-30%
	Second trimester 13-27 wks	+300 Kcal/day	+3.3g/kg/day	20-30%
	3rd trimester 28-40 wks	+300 kcal/day	5.8g/kg/day	20-30%
LACTATION				
	Total nutrient requirements	+500 kcal/day	+20g/day	20-30%

Source: *WHO, 2009*

All pregnant women need routine supplementation of iron and folic acid, minerals involved in building the skeleton- calcium, magnesium and phosphorus are in great demand, consumption of proteins of high biological value (animal products) whenever possible helps to achieve this.

Nutritional Management of Children

Infant and young child feeding in the context of TB

In the past, infants were sometimes separated from their mothers, at least until their mothers became noninfectious. Separation made breastfeeding and care by the natural mother impossible and put infants at risk of infection and malnutrition caused by artificial feeding.

These measures are no longer recommended.
Current recommendations for TB infected mothers are on the following principles:

- The best way to prevent infection in infants of infected mothers is timely and properly administered chemotherapy for the mother
- Exclusive breastfeeding for 6 completed months
- Introduction of adequate complementary food and continuation of breastfeeding up to 2 years or beyond.
- Provide Isoniazid Preventive Therapy (IPT) for high risk children who have no sign or symptoms of TB disease i.e.
  - All children aged under 5years
  - All HIV infected children

Infant and Young Child Nutrition (IYCN) in the context of TB/HIV

Breastfeeding is an unequalled way of providing ideal food for the healthy growth and development of infants. WHO recommends breastfeeding with appropriate use of anti-retroviral drugs for the mother and baby is the best option for overall well-being and survival

of HIV exposed children. All HIV positive pregnant women shall be put on HAART and the child will be put on prophylaxis for 12 weeks. However in special conditions replacement feeding may be considered if AFASS (Acceptable, Feasible, Affordable, Sustainable and Safe) criteria are met. (Rapid advice ART, 2014)

Breastfeeding in Drug Resistance -TB

A breastfeeding mother with DR-TB should receive a full course of anti-TB treatment, as timely and effective treatment is the best way to prevent transmission her baby. The mother and her baby should not be completely separated. However, if the mother is sputum smear-positive, the cooperation of a family member should be sought to primarily care for the infant until the mother becomes sputum smear-negative.

In cases where the mother has converted to smear negative the mother and infant may spend time together, in a well-ventilated area or outdoors. The mother should wear a surgical cloth mask during breastfeeding. Replacement feeding should only be considered in special conditions. (DR-TB guidelnes Kenya 2014, Egypt, TB 2007)

Breastfeeding should be given on demand and mothers supported to exclusively breast feed for 6months with a continuation to 24months. Babies staying away from their mothers should be fed on Expressed breast milk. However where this is not feasible due to drug toxicities e.g In drug resistance TB adequate information and support on replacement feeds should be given for six months

Dietary needs of children

The rapid growth periods of infancy and childhood can only be maintained if a child's nutrient intake is optimal.

Children with acute and chronic pulmonary disease need high energy and proteins because of the increased basal metabolic rate, catabolism and growth. The fact that children have limited stomach capacity and appetite makes it particularly challenging to meet the nutrient requirements. It is therefore necessary to modify and plan the diet carefully to ensure adequate intake of food. Pulmonary disease often adversely affects nutritional intake due to poor appetite, mal-absorption, exposing patients to malnutrition

Recommendations

- Six smaller meals per day are indicated instead of three.
- The meals should be appetizing in appearance, taste and provide enough energy and protein.
- Household ingredients such as sugar, vegetable oil, peanut butter, eggs and non-fat dry milk powder can be used in porridge, soups, or milk based-drinks to increase the protein and energy content without adding to the bulk of the meal.
- At least 500ml to 750ml of milk or yoghurt should be consumed daily to ensure adequate intakes of vitamin D and calcium.
- At least five to six servings of fruit and vegetables should be eaten per day. Pure fruit juice can be used to decrease the bulk of the diet. Approximately half a glass of fruit juice is equal to one serving of fruit.

- The best dietary sources of vitamin B6 (pyridoxine) are yeast, wheat germ, pork, liver, whole grain cereals, legumes, potatoes, bananas, and oatmeal.

Table 7.9: Management of uncomplicated under nutrition (wasting) using NACS/FBP Protocol

Client category	Diagnosis	Eligibility criteria[1]		Intervention package[2]	FBP exit criteria[3] & Actions
		Primary	Secondary		
Children: 6 – 23 months	Severe undernutrition	- WHZ < - 3.0 Z score Or - MUAC < 11.5 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+	- Infant and young child nutrition counseling - Therapeutic food: 37g/kg body weight/ per day of RUTF, ie 21 – 28 sachets per wk[d]O - One bottle per month of safe water solution (SWS) e.g. WaterGuard®	- WHZ = or > - 2.0 Z score - No oedema on 2 consecutive visits - Exit client from FBP & monitor progress
	Moderate undernutrition	- WFH < - 2.0 Z score Or MUAC between 11.5 – 12.5 cm	- Linked children	- Infant and young child nutrition counseling - Supplemental food e.g. 100gms FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	- Graduate when: WHZ = or > - 1.0 Z Score - Exit client from FBP & monitor progress
Children: 24– 59 months	Severe undernutrition	- WHZ < - 3.0 Z score Or - MUAC < 11.5 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+	- Young child nutrition counseling - Therapeutic food: 37g /kg body weight/per day of RUTF ie 21 – 35 sachets per wk - One bottle per month of safe water solution (SWS) e.g. WaterGuard®	- WHZ = or > - 2.0 Z score - No oedema on 2 consecutive visits - Exit client from FBP & monitor progress
	Moderate undernutrition	- WHZ < -2.0 Z score - MUAC between 11.5 – 12.5 cm	- Linked children	- Young child nutrition counseling - Supplemental food e.g. 200gms FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	- Graduate when WHZ = or > - 1.0 Z score - Exit client from FBP & monitor progress

Client category	Diagnosis	Eligibility criteria[1]		Intervention package[2]	FBP exit criteria[3] & Actions
		Primary	Secondary		
Children: 5 – 9 years	Severe undernutrition	- BMI for Age < - 3.0 Z score Or - MUAC < 13.5 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+	- Nutrition counseling - 276gms per day of RUTF ie 21 sachets per wk - Supplemental food eg 100gms FBF - One bottle per month of safe water solution (SWS) e.g. waterGuard®	- BMI for Age = or > - 3.0 Z score - No oedema on 2 consecutive visits - Switch to FBF prescriptions only
	Moderate undernutrition	- BMI for Age < -2.0 Z score - MUAC between 13.5 – 14.5 cm	- Linked children	- Nutrition counseling - Supplemental food e.g. 200gms FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	- Graduate when BMI for Age = or > - 1.0 Z score - Exit client from FBP & monitor progress
Children: 10 - 15 years	Severe undernutrition	- BMI for Age < - 3.0 Z score Or - MUAC < 14.5 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+	- Nutrition counseling - Therapeutic food eg 276gms per day of RUTF ie 21 sachets per wk - Supplemental food eg 300gms per day FBF - One bottle per month of safe water solution (SWS) e.g. WaterGuard®	- BMI for Age = or > - 3.0 Z score - No oedema on 2 consecutive visits - Switch to FBF prescriptions only
	Moderate undernutrition	- BMI for Age < -2.0 Z score Or - MUAC between 14.5 – 18.5 cm	- Linked children	- Nutrition counseling - Supplemental food e.g. 300gms per day FBF - One bottle per month of safe water solution (SWS) eg Water Guard®	- Graduate when BMI for Age = or > - 1.0 Z score - Exit client from FBP & monitor progress

Client category	Diagnosis	Eligibility criteria[1]		Intervention package[2]	FBP exit criteria[3] & Actions
		Primary	Secondary		
Children :15+ years Adults: 18 years and above	Severe undernutrition	- BMI for Age < - 3.0 Z score Or - MUAC < 14.5 cm - BMI < 16 kg/m² Or - MUAC < 16 cm Or - MUAC 16 - 18.5 cm with WHO stages 2 or 3 criteria - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+	- Nutrition counseling - Therapeutic food eg 276gms per day of RUTF ie 21 sachets per wk - Supplemental food eg 300gms per day FBF - One bottle per month of safe water solution (SWS) e.g. WaterGuard®	- BMI = or > 16 kg/m² - No oedema on 2 consecutive visits - Switch to FBF prescriptions only
	Moderate/Mild undernutrition	- BMI for Age < -2.0 Z score Or - MUAC between 14.5 – 18.5 cm - BMI 16 to < 18.5 kg/m² Or - MUAC between 16 – 18.5 cm		- Nutrition counseling - Supplemental food e.g. 300gms per day FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	- Graduate when BMI > 18.5 kg/m² on 2 consecutive months or BMI > 20 kg/m² - Exit client from FBP & monitor progress
Pregnant women	Severe undernutrition	- MUAC < 19 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+ - BMI < 20 kg/m²	- Maternal nutrition and infant feeding counseling - Routine ANC counseling, referral & follow up - Therapeutic food eg 276gms per day of RUTF ie 21 sachets per wk - Supplemental food eg 300gms per day FBF - One bottle per month of safe water solution (SWS)e.g. WaterGuard®	- - BMI = or > 20 kg/m² OR MUAC = or > 19cm and weight gain = or > 1.3 kg/month [e]O - - Switch to FBF prescriptions only

Client category	Diagnosis	Eligibility criteria[1]		Intervention package[2]	FBP exit criteria[3] & Actions
		Primary	Secondary		
	Moderate/ Mild undernutrition; Poor weight gainO;	MUAC between 19 – 23 cm And/or Low weight gain of < 1.3 kg/ month (Low gestational weight gain)	- BMI < 20 kg/m² - Failure to gain weight despite OI control & or ART	- Maternal nutrition and infant feeding counseling - Supplemental food e.g. 300gms per day FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	Graduate when: - BMI = or > 20 kg/m² & OR MUAC = or > 23cm - And if weight gain = or > than 1.3 kg/ month - Exit client from FBP & monitor progress
Post-Partum women (1st 6 months)	Severe undernutrition	- MUAC < 19 cm - Appetite test ü	- Visible wasting - Bilateral pitting edema -/+ - BMI < 20 kg/m²	- Maternal nutrition and infant feeding counseling - Routine Post-natal counseling, referral & follow up - Therapeutic food eg 276gms per day of RUTF ie 21 sachets per wk - Supplemental food eg 300gms per day FBF - One bottle per month of safe water solution (SWS)e.g. WaterGuard®	- - Steady weight gain after 6 wks And - MUAC = or > 19 cm Or BMI = or > 20 kg/ m² - No oedema on 2 consecutive visits Switch to FBF prescriptions only
	Moderate/ Mild undernutrition; Rapid weight loss	- MUAC between 19 – 23 cm And/or - Non intentional rapid weight loss of > 0.7 kg/month in normal & low BMI clients	- BMI <20 kg/ m² - Failure to gain weight despite OI control & or ART.	- Maternal nutrition and infant feeding counseling - Supplemental food e.g. 300gms per day FBF - One bottle per month of safe water solution (SWS) e.g. Water Guard®	Graduate when: - BMI = or > 20 kg/m² & Weight loss is < 0.5 kg/ month for 2 consecutive months; OR - BMI = or > 20 kg/m² and steady weight gain is observed on 2 consecutive months - Exit client from FBP & monitor progress

Substance use and abuse and Tuberculosis

Smoking has been shown to lower the level of vitamin C and B-carotene in plasma and decrease the bioavailability of selenium (6). Smoking, alcohol use and abuse increases oxidative stress. Oxidative stress is an imbalance between the production of free radicals and the ability of the body to counteract or detoxify their harmful effects through neutralization by antioxidants. Oxidative stress leads to many pathophysiological conditions in the body. Therefore foods rich in antioxidants (Vitamin A, C, E and selenium) are recommended. Refer to table on local sources of vitamins (Annex)

Macronutrient requirements

Anti-TB treatment may not be fully effective if other frequent conditions such as malnutrition are not properly addressed. The extraordinarily high pill burden that MDR-TBHIV patients may face also merits attention. These treatments could amount to more than 30 pills a day.
There is currently no evidence to suggest that the proportion of dietary energy from macronutrients (e.g. protein, carbohydrate and fat) is different for people with active TB than for those without TB. It is generally recommended that all people consume approximately 15–30% of energy as protein, 25–35% as fat and 45–65% as carbohydrate (9). However, special advice regarding fat intake might be required for individuals undergoing antiretroviral therapy or experiencing persistent diarrhea (10).

Therefore, in TB HIV Co-infection;

- Increased energy intake of about 20% to 30% is recommended for adults during periods of **symptomatic disease or opportunistic infection** (e.g. in TB HIV Co-infection), to maintain body weight.

In children energy intakes need to be increased by 50% to 100% over normal requirements experiencing weight loss.

Additionally, referral to a nutritionist/dietician should be done in cases that require specialized nutrition management or in patient care

Micronutrients requirements in TB HIV Co-infection

- To ensure micronutrient intakes at RDA levels, HIV-infected adults and children are encouraged to consume healthy diets.
- Nevertheless, dietary intake of micronutrients at RDA levels may not be sufficient to correct nutritional deficiencies in HIV-infected individuals.

The Kenya National Technical Guidelines for Micronutrient Deficiency Control recommends Vitamin A supplementation for tuberculosis among other conditions of public health concern (MOH, 2008). There is evidence that some micronutrient supplements, e.g. vitamin A, zinc and iron, can produce adverse outcomes in HIV-infected populations. It is reasonable to support the current WHO recommendations to promote and support adequate dietary intake of micronutrients at RDA levels whenever possible.

Table 7.10: Calories for Varying Levels of Kidney Failure

Nutritional Parameter	Normal kidney Function	Stage 1-4 CKD (Conservative management)	Stage 5 Hemodialysis	Stage 5 Peritoneal dialysis	Transplant
Calories (kcal/kg/d)	30 – 37 45–65%	35 kcal/kg/d: for ages less than 60yrs 30– 35 kcal/kg/d: for ages more than 60yrs	35< 60yrs 30 – 35 ≥ 60yrs	35< 60yrs 30 – 35 ≥ 60yrs (include calories from dialysate)	30 – 35 (initial) 25 – 30 (maintenance)
Proteins (g/ kg/d)	0.8	0.6 – 0.75 (50% HBV)	1.2 (50% HBV)	1.2 – 1.3 (50% HBV)	1.3 – 1.5 initial 0.8 - 1.0 maintenance
Fat % (total Kcal)	25 – 30%	Patients considered high risk for CVDs emphasis on PUFAs and MUFAs Cholesterol 250 – 300 mg/d	Patients considered high risk for CVDs emphasis on PUFAs and MUFAs Cholesterol 250 – 300 mg/d	Patients considered high risk for CVDs emphasis on PUFAs and MUFAs Cholesterol 250 – 300 mg/d	< 10% saturated fat
Sodium (mg/d)	2,300 mg/ day	2,000	2,000	2,000	Limited 2,000 – 3000 Monitor medication and BP
Potassium (mg/d)	4,700 mg/ day	Correlated to laboratory values < 2,000	2,000 - 3000	3,000 – 4,000	4,700 mg/day Monitor medication effect Monitor electrolytes
Calcium (mg/d)	1000 mg/ day	1,200	≤2,000 from diet and medication	≤2,000 from diet and medication	1,200
Phosphorus (mg/d)	1700mg/d	Correlated to lab values	800 – 1,000	800 – 1,000	1700 mg/day

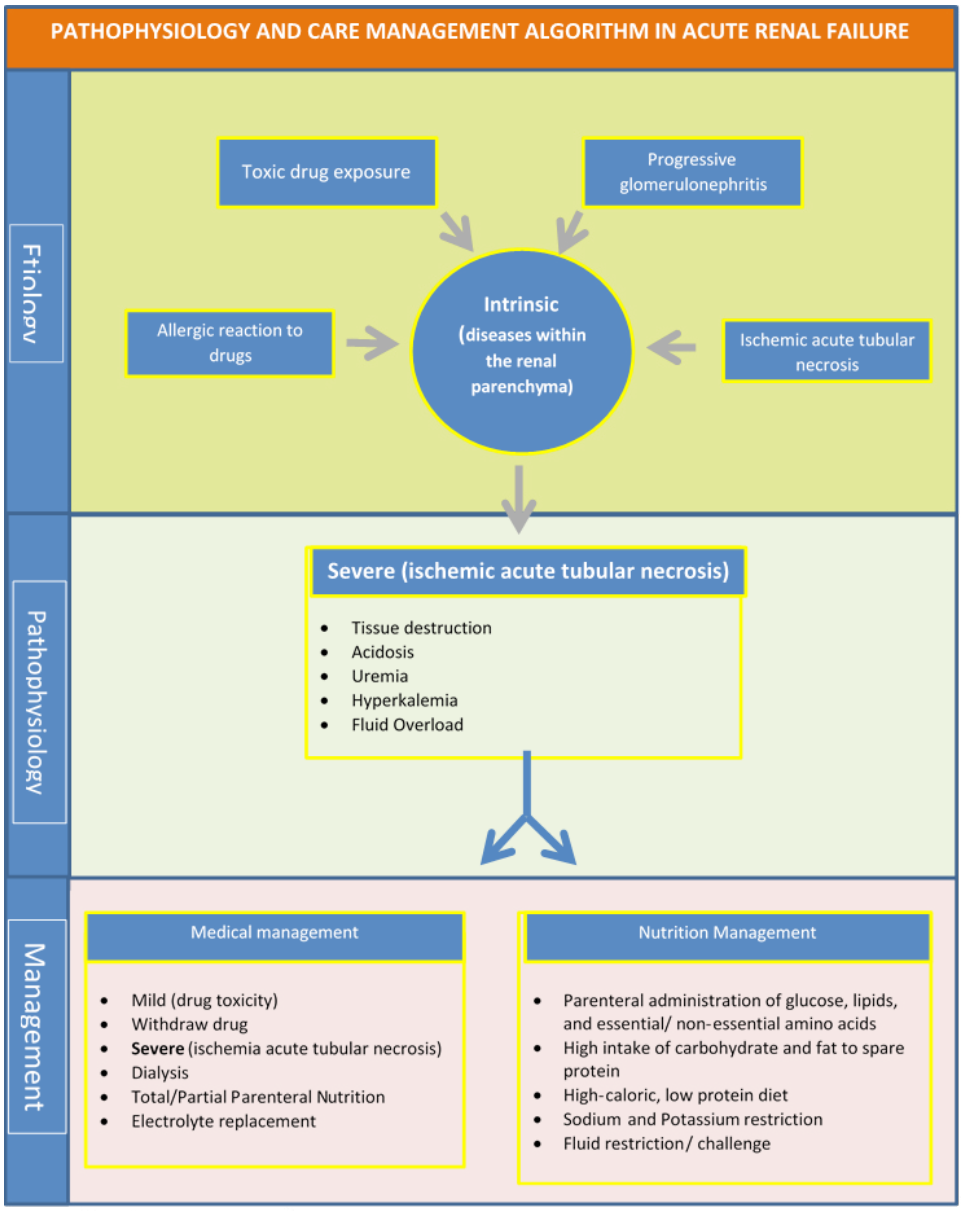
Fluids (ml/d)	2000 ml/d	Depends on 24 hr urine output +500 – 700ml/ day If NIL 500 – 700 ml/day Individualized based on CKD sage, oedema and hypertension	1,000 + urine output If NIL 500 – 700 ml/day	Monitored 1,500 – 2,000	2,000 – 3000 L/d
Vitamin D	5 – 15 mg/ day		0.25 mg/d		
Iron	8 – 18 mg/ day	100 mg weekly (IV	100 mg weekly (IV)	100 mg weekly (IV	8 – 18 mg/day Monitor levels
Erythropoietin	No need to supplement if kidney is working. Levels are normal	4,000 iu weekly (IV or IM)	4,000 iu weekly (IV or IM)	4,000 iu weekly (IV or IM)	Monitor levels Supplement if need be
Vitamin B6	25mg/day	25mg/day	50mg/day	50mg/day	25 mg/day
Vitamin B12	2.4 g/day	2.4 g/day	2.4 g/d	2.4g/day	2.4g/day
Folic acid	400g/day	400g/day	1000 mg/day	1000mg/day	800mg / day

Source: *(Foundation, 2004)*

In established under nutrition, Enteral nutritional and parenteral nutrition supplements are recommended. Intradialytic parenteral nutrition (IDPN) or intraperitoneal amino acids may be considered for selected cases if tube feeding is declined or clinically inappropriate (Foundation, 2004) (straton, 2005)) (Refer to in-patient management).
For adults with CKD (Stages Three to Five), the dose and timing of phosphate binders should be individually adjusted to the phosphate content of meals and snacks to achieve desired serum levels (Ikizler TA, 1996)
Other considerations:

- Nutrition assessments-biochemical assessment should be reviewed on every visit to check urea, creatinine, sodium and potassium.
- Referrals-any known cases of patients with kidney disease should be referred to a facility with a nephrology team and equipment.

Figure 7.5: Pathophysiology and Care Management Algorithm in Acute Renal Failure



Sourced from (Escott-Stump, 2008)

Nutrition Management in TB and Diabetes

Goals of nutrition therapy

- Attain and maintain blood glucose levels as close to normal as possible
- Prevent hypo- and hyperglycemia (Oral hypoglycemic may require the patient to increase the dosage.)
- Attain optimum blood lipids and blood pressure control and reduce the risk of macro vascular disease
- Assess energy intake to achieve optimum body weight (this can mean taking action to either increase or decrease body weight).
- Promote physical, social and psychological well being

- Prevent, delay or minimize the onset of chronic degenerative complications e.g. hypertension and renal diseases
- Achieve and maintain optimal metabolic and physiologic outcomes
- Provide relief from symptoms
- Individualize meal plan according to a person's lifestyle and based on usual dietary intake

Strategies for Effective Management

TB patients initiated on TB treatment with diabetes co-morbidity experience delayed recovery of body mass and haemoglobin, which are important for the functional recovery from disease.

- TB treatment leads to decreasing blood glucose levels 6 suggesting that integrated management of tuberculosis in people with high blood glucose could lead to better diabetes control.

Management

- Pyridoxine (Vitamin B6) is recommended during treatment of TB in patients with DM
- Review of DM treatment as a result of TB disease – TB like any other infection leads to impaired glucose control - Adjust dose of Oral Glucose Lowering Agents (OGLA). Some patients might have to switch to insulin during duration of TB disease.
- Close monitoring of blood glucose levels and appropriate adjustments done on the doses of OGLAs needed for adequate DM management.
- Individualized dietary modification is one of the cornerstones of diabetes management, and it is based on the principle of healthy eating in context of social, cultural and psychological influences of food choices. Dietary modification and physical activity are core in the management of newly diagnosed people with diabetes and have to be maintained.

Nutrition status monitoring and management needs to be done to ensure optimum management of the co-morbidities. This monitoring is especially important for patients whose nutritional indicators are approaching severe under-nutrition

Nutritional management of patients with co-morbidities

These physiological disorders either result from altered metabolism or affected metabolism. They include but are not limited to: - diabetes mellitus, hyper/hypothyroidism, hypertension, cardiovascular disorders.

Co morbidity with TB, TB/HIV further complicates their nutritional management. The table below highlights some of the conditions and gives nutritional recommendations that need to be considered in the overall management.

Table 7.11: Chronic Disease Conditions with TB/HIV and Nutritional Management

Condition	Nutrition management
Diabetes	• For undernourished patients with caution, hydrolyzed /elementary feeds are not recommended unless it is disease specific • Additional 200-500 Kcal (especially on patients on insulin) • Protein 1.2-1.5g/kg Bwt • Fats – 20g PUFA and MUFA • Supplementation of B6 • Vitamin A,C,E • Minerals zinc selenium, magnesium and calcium • Refer to diabetic clinic
Hyperthyroidism	• Treat the underlying cause • Use high calorie diet to meet the extra energy needs • Refer appropriately to medical/surgical clinic
Hypothyroidism	• Recommend iodine rich foods e.g. sea foods or iodine fortified salt • Refer appropriately
Hypertension	• Include foods high in potassium, magnesium, calcium and vitamin C • For undernourished patients give supplementary/therapeutic foods with caution • Refer to medical clinic
CVD	• Reduce salt intake to< 4g per day, an equivalent of (2400mg) sodium per day • Use a wide variety of fruits and vegetables • Refer appropriately

Source: *(MoMS, 2009)*

Note: Refer to the Kenya National Clinical Nutrition and dietetics Reference Manual (2010) or the Diabetes Educator manual.

Food drug interaction

Table 7.12: Side Effects Related to TB Drugs and Food Intake and Recommendations to Minimize Them

Drug name	Food recommendation	Avoid	Possible side effects
Rifampicin	To be taken I hr before or 2 after food. I hr before antacids	Alcohol	Nausea, vomiting, appetite loss
Isoniazid	Taken 1 hr before or 2 hrs after food. Give 10mg B_6 daily	Alcohol	Interferes with
Ethambutol	May be taken with food	Avoid alcohol	
Streptomycin	Increase fluid intake		Taste changes, taste of food, nausea
Pyrazinamide	May be taken with food		

Ethionamide	Take with or after meals(Supplement with Vit B_6)	Alcohol	Abdominal discomforts, nausea
Ofloxacin	Take 2hrs before or after food	Antacids, milk products	Gastrointestinal reactions, Insomnia
Kanamycin (Km)	Can be taken without regard to food		Ototoxicity: hearing damage, vestibular, disturbance, Nephrotoxicity: deranged renal function test
Capreomycin	Increase fluid intake, take with foods high in potassium(bananas, avocados)		Ototoxicity: hearing damage, vestibular, disturbance, Nephrotoxicity: deranged renal function test
Para-aminosalicylic acid(PAS)	Take with or immediately after food. Increase fluid intake	Alcohol	Gastrointestinal reactions Dizziness, Headache, Depression, Memory loss
Cycloserine	Supplement with vitamin B_6	Alcohol	Dizziness, Headache, Depression, Memory loss

CHAPTER
8

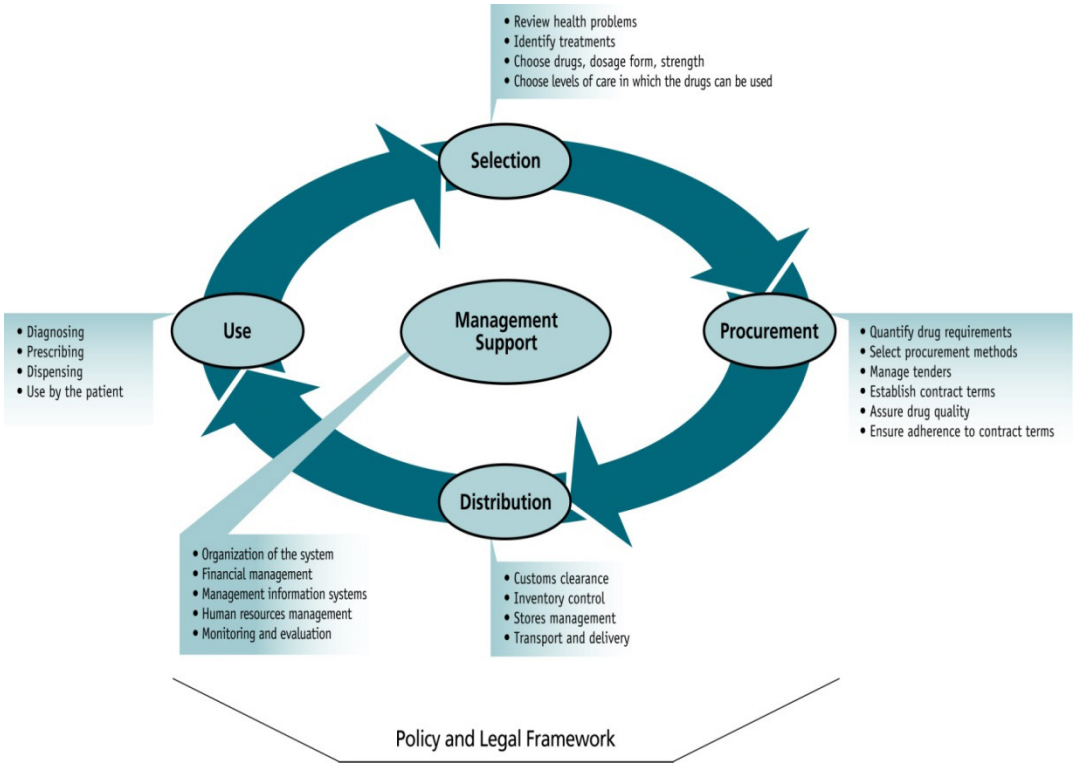
NTLD-P COMMODITIES SUPPLY CHAIN MANAGEMENT PHARMACEUTICAL MANAGEMENT

Pharmaceutical management is a set of practices aimed at ensuring the timely availability and appropriate use of safe, effective, quality medicines and related products and services in any health-care setting.

The Pharmaceutical Management Cycle

The Pharmaceutical Management Cycle is a systematic approach to ensure that medicines at all levels of health care delivery are consistently available and appropriately used. It emphasizes the connections between four drug management activities - selection, procurement, distribution and use.

Figure 8.1: The pharmaceutical Management Cycle



The cycle was developed by the Management Sciences for Health' Centre for Pharmaceutical Management in collaboration with the World Health Organization's Action Program on Essential Drugs.

Quantification of Anti-Tuberculosis Medicines

Quantification is the process of estimating the quantities of anti-tuberculosis medicines and other commodities needed for a specific period of time in order to ensure an uninterrupted supply. Quantification is an important step in procurement and ordering for re-supply. Good quantification ensures the appropriate allocation of funds to enable purchase of the right medicine in the right quantity at the right time.

The rationale for quantification of anti-tuberculosis medicines and other commodities

- To ensure that there are sufficient quantities to meet clients' / patients' needs and avoid shortages/stock-outs.
- To avoid surpluses that may lead to over-stocking, expiries and/or wastage of commodities.
- To make informed procurement adjustments when faced with budgetary constraints.

NTLD-Program Commodities

First line TB medicines

- Adult TB Medicines: Patient packs (RHZE/RH), RHZE, RHE and Streptomycin 1gm injection.
- Children: RHZ (75,50,150mg) tablets, RH (75,50mg) tablets and Ethambutol 100mg tablets
- Isoniazid Preventive Therapy:
    - Isoniazid

Table 8.1: Second Line (DRTB) Medicines

Class	Medicines name
Injectables	**Capreomycin1gm, Kanamycin 1gm, Amikacin 1gm injection**
Oral bacteriostatics / bactericidal medicines	• Fluoroquinolones; Ofloxacin, Levofloxacin and Moxifloxacin • Protionamide (Pto) • Cycloserine (Cs) • P-aminosalicylic acid (PAS) • Pyrazinamide • Terizidone • Meropenem • Amoxycillin/Clavulanic acid • Clarithromycin • Clofazimine • Linezolid
• **XDR TB Medicines**	• Bedaquiline • Delaminid • Clofazimine • Linezolid
Other medicines	• Assorted Ancillary medicines • Pyridoxine 25mg & 50mg tablets

Laboratory consumables for AFB microscopy

- Assorted commodities
- Diagnostic equipments

Nutrition

- Ready to Use Therapeutic Food (RUTF)
- Ready to Use Supplementary Foods (RUSF)
- Fortified Blended Flours (FBF)
- Safety net food basket
- Other

Monitoring & Evaluation

- M&E tools
- LMIS tools

Advocacy, Communication and Social Mobilization

- Guidelines
- Tools (IEC materials, community tools etc)
- Other tools

Equipment

- Arthropometric equipments (adult and baby weighing scales)
- Laboratory equipments (Microscopes, Weighing machines etc).

Quantification Methods

This guideline focuses attention on the two most commonly used methods—consumption and morbidity. The particular method used depends on the type of data available. The main methods of quantification include:

a) Consumption method

The consumption based method uses historical data on the actual medicines dispensed to patients to calculate the quantity of medicines that will be needed in the future. When using the consumption method for quantification, out of stock periods must be adjusted in the calculation.

b) Morbidity method

The morbidity-based method uses data about diseases and the frequency of their occurrence in the population (incidence or prevalence) or the frequency of their presentation for treatment. It forecasts the quantity of drugs needed for the treatment of specific diseases, based on projections of the incidence of those diseases.

Quantification tools used to quantify commodities

- Quant-TB quantification tool
- GDF quantification tool
- Excel sheet

Good inventory management

An inventory management system is a cycle of activities comprising ordering, receiving, storage and issuing of anti-tuberculosis medicines.

a) Ordering

The facility orders supplies monthly from the district store using a standard order form (FCDRR). The district orders supplies monthly from KEMSA stores using an electronic district aggregation tool which also serves as a report.

b) Receiving

The facility receives supplies; counter checks against the standard order form and delivery note, and record's the transaction on a stock card.

c) Storage

Anti-tuberculosis commodities should be stored in optimal conditions to ensure their safety and efficacy in accordance with the principles of good storage practices:

- Good arrangement
- Quality maintenance
- Assured security
- Good inventory control and stock rotation
- Good record keeping

Disposal of unusable stock should be carried out according to the guidelines for disposal of pharmaceuticals. Some commodities like PAS require cold storage and maintenance of the cold chain is important to maintain their efficacy.

d) Issuing

The facility issues supplies to various points of use, using an issue/requisition voucher (S11/S12) and records the issue on the bin card. Commodities will be issued using "first expiry, first out" or "first in first out" (FEFO/FIFO) principle. This will guide in proper stock control and management

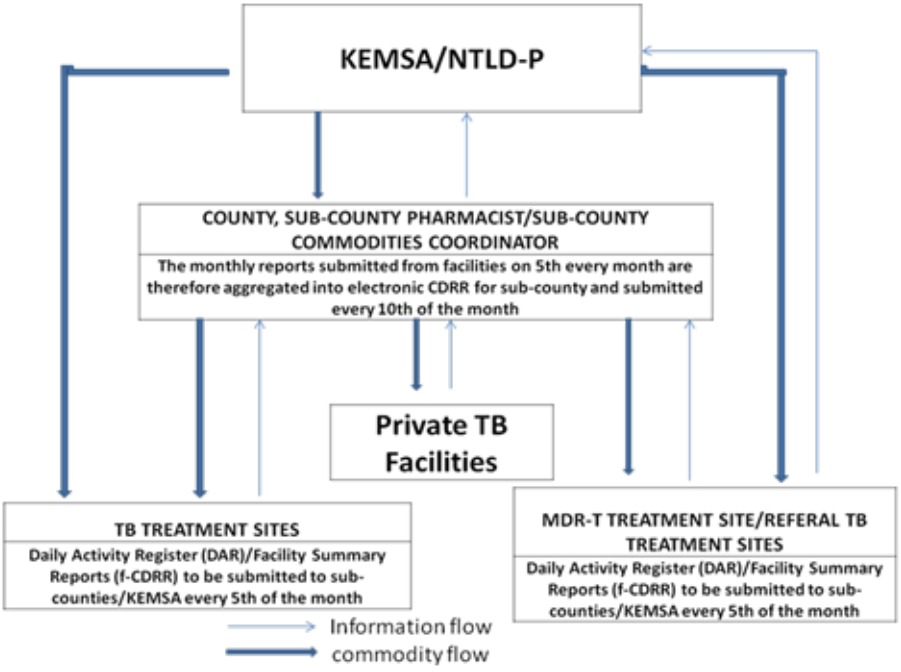
Types of inventory records

Various forms are used for requisitioning and issuing medicines, financial accounting, and preparing consumption and stock balance reports.

Table 8.2: Type of Inventory Records

Record type	Source document	Information
Stock keeping records	Bin cards, stock ledger card	Stock at hand Receipts, losses and adjustments
Receiving and storing commodities	• Delivery Notes Bin cards/stock ledger	Confirmation of delivery and receipt of commodities
Issuing	Bin cards • S11/S12	Issues to dispensing area or other facilities
Dispensing	TB Daily activity registers (DAR)	Amount of commodities actually dispensed to patients
Reporting & Ordering	**At facility:** TB f-CDRR (facility to sub-county) **At sub-county level:** E-CDRR, KEMSA web-based report	The consumption/dispensed to user data. Stock balances at end of each reporting period

Figure 8.2: Flow of logistic Management Information



Definitions of Key Inventory Management Terms

- **Average monthly consumption**: this refers to the average quantity of commodities consumed per month.
- **Months of stock:** the quantity on hand expressed as the number of months that quantity should last calculated based on the commodity's average monthly consumption.
- **Lead time:** the time interval between when a new stock is ordered and when it is received and available for use.

- **Review period**: The routine interval of time between assessments of stock levels to determine if an order should be placed. It is also known as order interval or re supply interval.
- **Maximum stock level:** the amount of stock above which a facility should not exceed under normal circumstances
- **Minimum stock level:** the amount of stock below which a facility should not fall under normal circumstances
- **Shelf life**: the length of time a product may be stored without compromising its usability, safety, purity or potency.
- **Pipeline:** the entire chain of storage facilities and transportation links through which supplies are moved from manufacturers to clients
- **Stock out:** Non availability of any ACT for 2 consecutive days in a month.

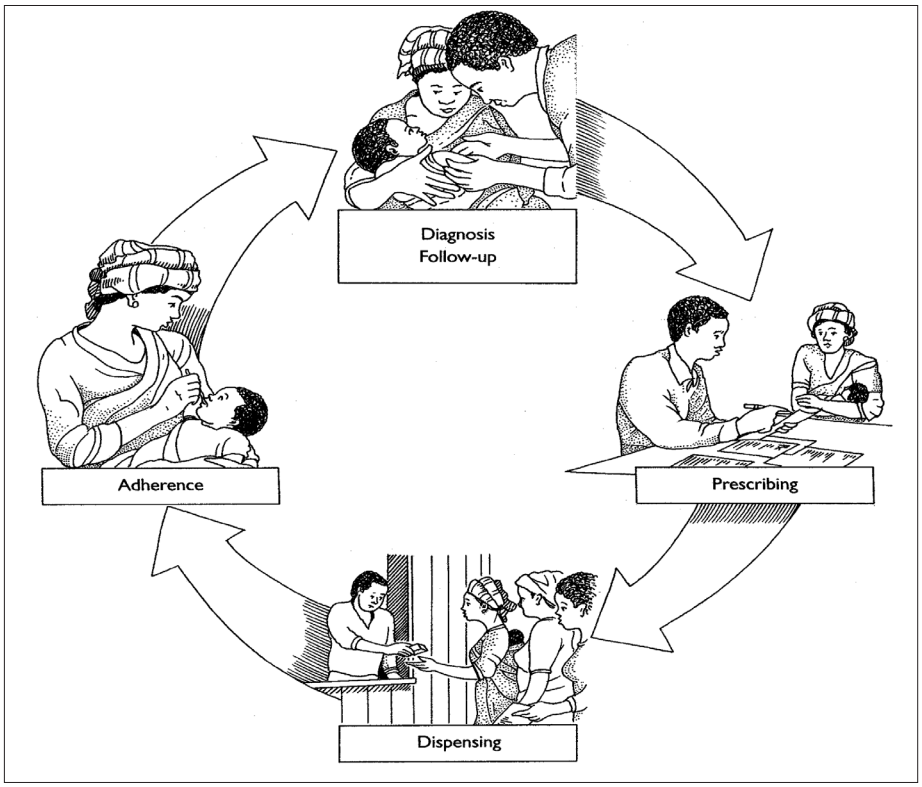
Monitoring & Evaluation Indicators

- National reporting rate
- Proportion of health facilities having a total stock out of Tb patient packs

Rational Use of Anti-Tuberculosis Medicines

Rational Drug Use (RDU) requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community (World Health Organization, 1988).

Figure 8.3: The medicine use cycle



Importance of RDU

- Irrational medicine use can destroy the benefits of a good pharmaceutical management system and also reduce the therapeutic useful life of an effective medicine.
- Resources spent on procurement are lost if the correct drugs are not prescribed and dispensed to the correct patient.

Factors affecting rational use of medicines

- **Diagnosis** - correct diagnosis based on parasitologically confirmed diagnosis
- **Prescribing** – prescribing /administering the recommended medicine based on the correct diagnosis
- **Dispensing** - correct dispensing (quantity, packaging and labeling) of the prescribed medicine.
- **Patient compliance** - patients' adherence to health worker and label instructions.

Minimum dispensing information

a) Instructions on how to take the drug with DOT
b) Instructions on how long to take the medicine
c) Report any suspected ADR
d) Clear label with appropriate patient and medicine information

Pharmacovigillance

Definitions of key terms

Pharmacovigillance: WHO defines pharmacovigilance as the science of collecting, monitoring, researching, assessing and evaluating information from healthcare providers and patients on the adverse effects of medicines, biological products, herbals and traditional medicines, with the view to identifying new information about hazards, and preventing harm to patients.

An ADR is a response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function.

Adverse event: Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Side effect: Any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the drug.

Counterfeits: WHO defines a counterfeit pharmaceutical product as a product that is deliberately and fraudulently mislabeled with respect to identity and / or source.

Three methods of pharmacovigillance

a) **Spontaneous reporting** is the most common form of PV is spontaneous (also called voluntary) which involves a health-care worker - or even the patient - reporting a drug-related reaction. The effectiveness of such systems very much depends on the patient volunteering this information (people have different thresholds when they decide to approach formal careers for reporting), on health-care workers' competence to recognize an event, and their motivation to report it. Episodes of suspected adverse drug reactions linked to the use of drugs are reported voluntarily by health care workers or patients to the designated body responsible for pharmacovigillance within the country (i.e. the national pharmacovigillance centre (NPVC)) at the Pharmacy and Poisons Board.

b) **Targeted spontaneous reporting** uses a methodology that monitors and records all or a specific set of safety concerns in a defined population of treated patients, e.g. drug resistant TB patients on treatment.

c) **Active PV** is a more systematic and proactive form of safety surveillance. In active PV, events are elicited as part of patient monitoring using a set of questions and an array of laboratory/clinical tests at defined periods of time, before, during and after treatment. The records from active PV make it possible to determine the exact number of patients monitored and exposures to a drug; they also enumerate the events related to an exposure, in a similar way to what one would do in a longitudinal epidemiological study. Cohort event monitoring (CEM) is one of the standard methods of active PV which is used to monitor adverse events in patients who receive a particular medication or treatment regimen. Patients are followed up prospectively in groups and all adverse events are registered during treatment and usually for a given time after its end. **The CEM method** is the form of active PV which has been best defined and used in different settings, both well resourced and low income. Beyond its role as part of a risk management plan, CEM can provide useful insights into the patterns of utilization and the adoption of a new drug in clinical practice (e.g. acceptability by clinicians and patients)

Ultimate goals of Pharmacovigillance are:

- The rational and safe use of medicines
- The assessment and communication of the risks and benefits of drugs on the market
- Educating and informing patients

Adverse experiences with medication
Report ALL suspected adverse experiences with medications, especially those where the patient outcome is:

- Death
- Life-threatening (real risk of dying)
- Hospitalization (initial or prolonged)
- Disability (significant, persistent or permanent)
- Congenital anomaly
- Required intervention to prevent permanent impairment or damage

Report and adverse experience even if:

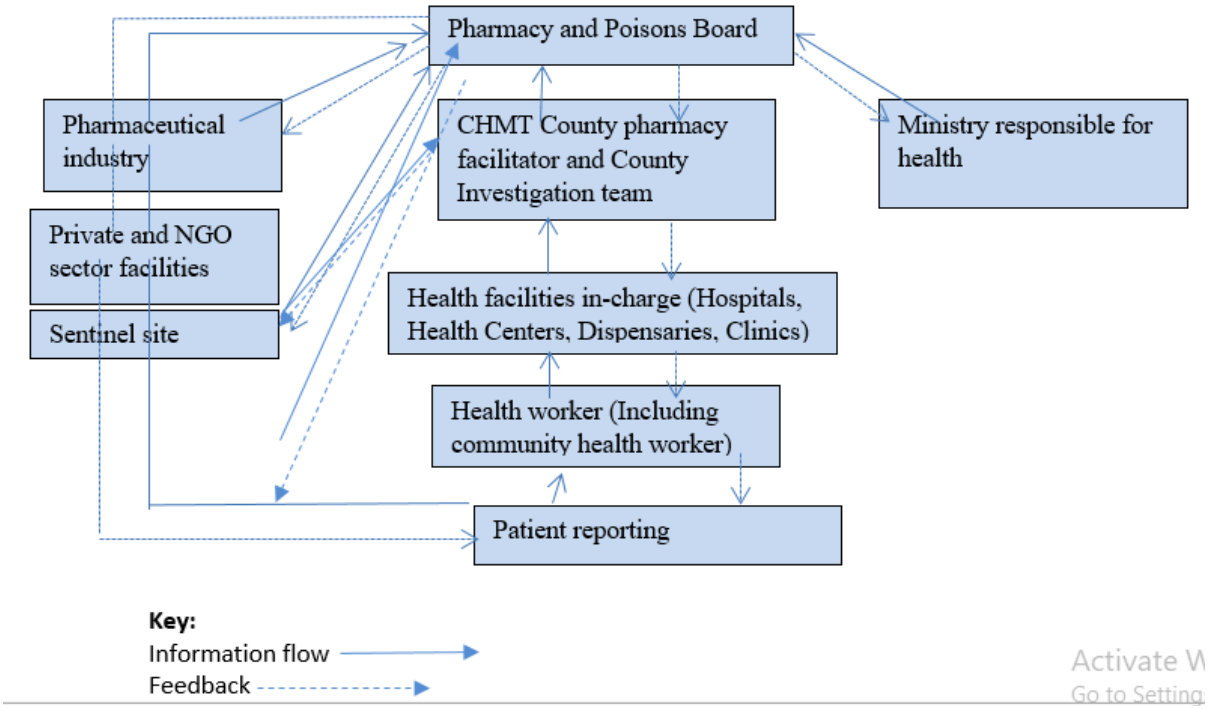
- You are not certain if the drug caused the reaction
- You do not have all the details

Tools and information flow

Reporting of ADRs is done using:

- Yellow form (PV 1) - form to capture all suspected adverse drug reactions
- White card (PV 4) - Alert card for life threatening drug reactions
- Pink form (PV 6) - form for reporting poor quality medicinal products

Figure 8.4: Flow of pharmacovigilance information



Feedback to all levels of the system is the responsibility of the Pharmacy and Poisons Board. This could take the form of:

- Recall – a withdrawal of affected product batches from the market
- Labeling change – inclusion of new information
- Reschedule – change of the regulatory class e.g. POM to OTC
- Withdrawal – removal of product from the market
- Policy change – e.g. change of use of SP from uncomplicated malaria to use in IPT prophylaxis

Introduction and Use of Bedaquiline

Mode of action

Bactericidal: Inhibits ATP synthesis; novel method of action; The drug has a 5.5-month half-life. CYP3A4 is the major CYP isoenzyme involved in the metabolism of bedaquiline. The metabolism leads to the formation of N-monodesmethyl metabolite (M2). M2 is not thought to contribute significantly to clinical efficacy given its lower average exposure (23–31%) in humans and lower antimycobacterial activity (4- to 6-fold lower) compared to the parent compound. M2 concentrations appeared to correlate with QT prolongation. Bedaquiline is mainly eliminated in faeces. The renal clearance of unchanged drug is insignificant

Minimal requirements for introduction of Bedaquiline

- Identify patients eligible for treatment with Bedaquiline
- Informed consent from patient (or guardian if patient is below 18 years of unsound mind/health)
- Clinical Review Committee consultation
- Treatment initiation
- Monitoring treatment response
- Pharmacovigilance: detection, management and reporting of adverse events
- Individual drug resistance monitoring

Outcome Indicators Reported in Pharmacovigilance of Bedaquiline
Many of the outcome indicators will be collected as part of routine recording and reporting, as discussed in the previous sections.

Safety outcome indicators

These include percentage of patients receiving bedaquiline who develop

- Serious adverse events (particularly related to heart and liver)
- Bedaquiline associated adverse drug reactions; and
- Time to development of bedaquiline-associated adverse drug reactions

Efficacy outcome indicators

- Percentage of patients on bedaquiline with successful treatment outcomes (cure and completed treatment); Percentage of patients on bedaquiline with unsuccessful treatment outcomes (treatment failure, lost to follow-up and death)
- Average time to sputum culture conversion
- Percentage of patients treated with bedaquiline who developed resistance to the medication

Tolerability outcome indicators

- Percentage of patients defaulting from treatment;
- Number of missed doses of bedaquiline in the six-month treatment period; and
- Qualitative assessment of the patients' experience with bedaquiline

Treatment Initiation for Bedaquiline

After approval by the Clinical Review Committee, the patient can be started on treatment. Baseline data to be collected at treatment initiation include those collected for patients under PMDT. In addition, information on the reasons for bedaquiline prescription, baseline ECG results, and presence of a signed informed consent should be documented. The routine second-line treatment card should be used, and a system for identifying patients on bedaquiline should be developed (such as coloured highlighting, tabs in e-databases). Bedaquiline must be used for a maximum length of 24 weeks (six months) at the start of treatment in addition to the WHO-recommended MDR-TB regimen, which generally lasts for about 20 months

Note: With XDR-TB, the total treatment can be extended to 24 months; however, bedaquiline is still used only in the initial six months.

Warning: Bedaquiline should not be introduced into a regimen in which the other companion drugs are known or believed to be ineffective or are failing to show effectiveness. This implies that bedaquiline should not be added alone to a failing regimen, and should be introduced well before the regimen fails completely.

Bedaquiline is available as 100 mg tablets. Bedaquiline must be taken at the recommended dose and indicated frequency of administration. The six-month dosing schedule of the medication is as follows:

- **Week 0–2**: Bedaquiline 400 mg (four tablets of 100 mg) daily (seven days per week)
- **Week 3–24**: Bedaquiline 200 mg (two tablets of 100 mg) thrice a week (with at least 48 hours between doses) for a total dose of 600 mg per week
- **Week 25 (start of month seven) to end of treatment**: Continue other second-line anti-TB drugs only, as per WHO standard recommendations. Bedaquiline is NOT used in this phase of treatment
- Bedaquiline can be taken together with other anti-TB drugs and should be taken with a light meal (bedaquiline is better absorbed with food**).* Currently, dose adjustment is not a requirement in any circumstance**, even if concomitant agents are known to affect bedaquiline bioavailability.
- **Missed doses**: If a dose is missed during the first two weeks of treatment, patients should not make up the missed dose but should continue the usual dosing schedule.
    - From week three if a 200 mg dose is missed, patients should take the missed dose as soon as possible, and then resume the thrice weekly regimen
- Administration of MDR-TB treatment containing bedaquiline (hospital-based or outpatient-based) should be arranged according to the treatment protocol and country policy.
- For HIV-positive patients on antiretroviral treatment, **consideration should be given to potential drug interactions and overlapping toxicities** between bedaquiline and antiretroviral drugs. Therefore, caution should be used when designing regimens for patients on antiretroviral treatment .
- At the time of treatment initiation and during follow-up visits, relevant patient details, comorbidities, laboratory test results and adverse events need to be collected. PMDT forms already in use should be adapted to incorporate additional data fields required for

- In addition, patients on bedaquiline should be seen at least on a monthly basis while they are receiving the drug. Patient monitoring should include:
    - Clinical evaluation (daily if the patients is hospitalized; weekly if on outpatient model of care during the intensive phase; then monthly after the patient has stabilized on bedaquiline).
    - Weight (baseline, then every two to four weeks)
    - Height (baseline, then monthly only for children)
    - Treatment adherence and tolerance to drugs (i.e. regular check of treatment card)
    - Laboratory tests to assess response to TB therapy:
        - Sputum smears and culture (ideally every month throughout the treatment)
        - DST at baseline – should be repeated if patient remains positive or reverts to positive culture after month four
        - Laboratory tests to check for adverse events, including creatinine, electrolytes, thyroid function, liver function, complete blood count, audiometry, visual acuity and ECGs. The timing of these routine assessments should be determined as necessary
        - Chest radiograph: baseline, then every six months

Use of Bedaquiline in special circumstances

Use in pregnancy/breastfeeding: Not recommended during pregnancy or breastfeeding due to limited data. Reproduction studies performed in rats and rabbits have revealed no evidence of harm to the fetus. Use in renal disease: No dosage adjustment is required in patients with mild to moderate renal impairment (dosing not established in severe renal impairment, use with caution).

Use in hepatic disease: No dosage adjustment is required in patients with mild to moderate hepatic impairment. Dosing and toxicity not well established in severe hepatic impairment, use with caution and only when the benefits outweigh the risks.

Table 8.3: The Common Side Effects, Likely Causing Agents, And Suggested Management Strategies

Classification	Name of Drug	Daily Dosage		Side-effects	
Group	Drugs	Adult and child (mg/kg)	Adult dosage	Common	Uncommon
Group 1: First-line oral anti-TB agents	Isoniazid (H)		300 mg	Hepatitis, Cutaneous hypersensitivity, Peripheral neuropathy	Giddiness, Convulsion, Optic neuritis, Mental symptoms, Haemolytic anaemia, Aplastic anaemia, Lupoid reactions, Arthralgia, Gynaecomastia
	Rifampicin (R)		450 mg (<50 kg) 600 mg (≥ 50 kg)	Hepatitis, Cutaneous hypersensitivity, Gastrointestinal reactions, Thrombocytopenic, purpura, Febrile reactions, "Flu syndrome"	Shortness of breath, Shock, Haemolytic anaemia, Acute renal failure

	Ethambutol (E)	25	800 mg-1.2 g (<50 kg) 1.2-1.6 g (≥ 50 kg)	Retrobulbar neuritis, Arthralgia	Cutaneous reaction, Peripheral neuropathy
	Pyrazinamide (Z)	30-40	1.0-1.5 g (<50 kg) 1.5-2.0 g (≥ 50 kg)	Hepatitis, Nausea, Vomiting, Arthralgia,	Sideroblastic anaemia
Group 2: Injectable anti-TB agents	Streptomycin (S)	15-20(adult) 20-40 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Cutaneous hypersensitivity, Giddiness, Numbness, Tinnitus, Vertigo, Ataxia, Deafness	Renal damage, Aplastic anaemia
	Kanamycin (Km)	15-30 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular, disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
	Amikacin (Am)	15-22.5 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular, disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
	Capreomycin (Cm)	15-30 (child)	500-750 mg (<50 kg) 1g (≥ 50 kg)	Ototoxicity: hearing damage, vestibular, disturbance, Nephrotoxicity: deranged renal function test	Clinical renal failure
Group 3: Fluoroquinolones	Ofloxacin (Ofx)	15-20 (child)	800 mg	Gastrointestinal reactions, Insomnia	Anxiety, Dizziness, Headache, Tremor, Convulsion
	Levofloxacin (Lfx)	7.5-10 (child)	750 mg	Gastrointestinal reactions, Insomnia	Anxiety, Dizziness, Headache, Tremor, Convulsion
	Moxifloxacin (Mfx)	7.5-10 (child)	400 mg	Gastrointestinal reactions, Insomnia	Dizziness, Restlessness, Diarrhea
Group 4: Oral Bacteriostatic 2nd line anti-TB agents	Ethionamide (Eto)	20-May	500 mg (<50 kg) 750 mg (≥ 50 kg)	Gastrointestinal reactions	Hepatitis, Cutaneous reactions, Peripheral neuropathy
	Protionamide (Pto)	20-May	500 mg (<50 kg) 750 mg (≥ 50 kg)	Gastrointestinal reactions	Hepatitis, Cutaneous reactions, Peripheral neuropathy
	Cycloserine (Cs)	0-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Dizziness, Headache, Depression, Memory loss	Psychosis, Convulsion
	P-aminosalicylic acid (PAS)	150	8 g	Gastrointestinal reactions reactions	Hepatitis, Drug fever, Hypothyroidism, Haematological
	Terizidone	15-20	500 mg (<50 kg) 750 mg (≥ 50 kg)	Dizziness, Headache, Depression, Memory loss	Psychosis, Convulsion

XDR TB Medicines	Bedaquiline	Not indicated	Week 0–2: (400mg) Week 3–24: (200mg) >24week (continue with other treatment regimen	Nausea* Anorexia* Chest pain* Transaminases increased* Chest Pain* Anorexia* Rash* Headache Blood amylase increased Hemoptysis	**Warnings and Precautions** - QT Prolongation

Warnings and Precautions On Use Of Bedaquiline

- **QT Prolongation**: BDQ prolongs the QT interval. An electrocardiogram (ECG) should be obtained before initiation of treatment, and at least 2, 12, and 24 weeks after starting treatment with BDQ. Serum potassium, calcium, and magnesium should be obtained at baseline and corrected if abnormal. Follow-up monitoring of electrolytes should be performed if QT prolongation is detected. The following may increase the risk for QT prolongation when patients are receiving BDQ, and therefore ECGs should be monitored closely:
- Use with other QT-prolonging drugs including fluoroquinolones and macrolide antibacterial drugs and the antimycobacterial drug, clofazimine
- A history of Torsade de Pointes
- A history of congenital long QT syndrome
- A history of hypothyroidism and bradyarrhythmias
- A history of uncompensated heart failure
- Serum calcium, magnesium, or potassium levels below the lower limits of normal
    - **BDQ treatment (and all other QT-prolonging drugs) MUST be DISCONTINUED if the patient develops**:
    - Clinically significant ventricular arrhythmia
    - A QTcF interval of >500 ms (confirmed by repeat ECG)
    - Monitor ECGs frequently to confirm that the QTc interval has returned to baseline

If syncope occurs, obtain an ECG to detect QT prolongation

Patients with a history of ventricular arrhythmias or recent myocardial infarction MUST be evaluated by a cardiologist before starting on BDQ

- **Drug Interactions**
    - **CYP3A4 Inducers/Inhibitors**: BDQ is metabolized by CYP3A4 and its systemic exposure and therapeutic effect may therefore be reduced during co-administration with inducers of CYP3A4 and increased during co-administration with inhibitors of CYP3A4

- Co-administration of BDQ and rifamycins (rifampin, rifapentine, and rifabutin) or other strong CYP3A4 inducers used systemically should therefore be avoided

  Co-administration of BDQ with strong CYP3A4 inhibitors may increase the systemic exposure to SIRTURO™, which could potentially increase the risk of adverse reactions, and therefore the use of SIRTURO™ and strong CYP3A4 inhibitors used systemically for more than 14 consecutive days should be avoided,.e antidepressants, antifungals (Ketoconazolem Itraconazole), antivirals (atazanavir, indinavir, nelfinavir, ritonavir, sequinavir), Macrolide antibiotics, Other agents (grape fruit juice)

Table 8.4: The Common Side Effects, Likely Suspected Agents And Suggested Management Strategies

Side affect	Suspected agent(s)	Suggested management strategy	Comments
Seizures	Cs H FQ	• Suspend suspected agent • Initiate anticonvulsant therapy (e.g. carbamazepine) • Restart suspected agent or reinitiate suspected agent at lower dose**, if essential** to the regimen	• Continue anti depressants to until treatment is completed
Peripheral neuropathy	CS H FQ KM AMK CM E, Ethio	• Increase pyridoxine to maximum daily dose (**200 mg per day**). • **Change** parenteral to CM if patient has documented susceptibility to CM. • Initiate tricyclic antidepressants e.g. amitriptyline. NSAIDS • Lower dose of suspected agent, if this can be done without compromising regimen.	• Patients with co-morbid disease (e.g., diabetes, HIV, alcoholism) may be more likely to develop peripheral neuropathy. • Neuropathy is irreversible; some patients may experience improvement when offending agents are suspended.
Hearing loss	S KM AMK CM	• Change parenteral to CM if patient has documented susceptibility to CM • Injectible should never be stopped before conversion of patients	• Audiometry at the initiation of MDR TB therapy. • Hearing loss is **generally not** reversible.
Psychotic symptoms	Cs, H, FQ, Mfx Ethio	• Usually caused by Cs. Withhold suspected agents till symptoms are brought under control. • Initiate anti-psychotic drugs e.g. Haloperidol	• Continue anti-psychotic treatment throughout MDR TB therapy. • Prior history of psychiatric disease is **not a contraindication Second line drugs**

Side affect	Suspected agent(s)	Suggested management strategy	Comments
		• Start Cycloserine at 250mg per day, observe for 5 days. If stable increase to 250mg BD for 5 days. Increase the dose again to 750mg per day. If patient can't tolerate, reduce to where the pat can tolerate. **NB. Cycloserine is given in divided doses.** • In case of severe psychosis, replace with PAS	• Psychotic symptoms **are generally reversible** upon completion of MDR TB treatment or cessation of the offending agent
Depression	Socio-economic circum-stances, chronic disease, CS, FQ H, Ethio	• Improve socioeconomic conditions. • Group or individual counseling. • Initiate antidepressant drugs. • Lower dose of suspected agent, if this can be done without compromising the regimen.	• Socioeconomic conditions &chronic illness are contributing factors to depression. • Depressive symptoms may fluctuate during therapy • History of prior depression is not a contraindication to the use of the Second line drugs
Hypo-thyroids	PAS Pto/Ethio especially when given in combination	• Initiate thyroxine therapy. • Thyroxine should be given for till one month after completion of treatment • Follow TSH and adjust thyroxine periodically	• **Completely reversible** upon discontinuation of PAS or Ethio.
Nausea and vomiting	PAS Pto, H, E Z, CFZ, BDQ	• Rehydrate • Initiate anti-emetic therapy. • Take medication after meals Monitor electrolytes especially potassium and replace	• Nausea and vomiting are common in early weeks of therapy and usually **abate** with time supportive therapy. • Reversible upon discontinuation of suspected agent.
Gastritis	PAS, Pto/Ethio H, E Z CFZ	• Antacids (e.g., calcium carbonate, H2-blockers, proton-pump inhibitors). • Dosing of antacids should be taken two hours before or after anti-TB medications.	• Severe gastritis, as manifested by hematemesis, melena, or hematechezia, is rare. • Reversible upon discontinuation of suspected agent(s).

Side affect	Suspected agent(s)	Suggested management strategy	Comments
Hepatitis	Z, R, H Pto/Ethio PAS, E FQ BDQ	• Stop all therapy pending resolution of hepatitis. (*If the LFT results shows a >5 times more than the reference range*) • Rule out other potential causes of hepatitis. • Re-introduce remaining drugs, one at a time with the **LEAST** suspected hepatotoxic agents first, while monitoring liver function	
Renal failure	S KM AMK CM	• CM if an aminoglycoside had been the prior parenteral in regimen. • Use intermittent dosing while monitoring the creatinine clearance • Adjust all TB medications according to the creatinine clearance	• History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure.
Electrolyte dis-turbance (Hypo-magnesaemia & Hypokalemia	CM KM AMK S	• Check potassium. • If potassium is low, also check magnesium (and calcium if hypocalcaemia is suspected). • Replace electrolytes as needed as per guideline	• **If severe hypokalemia is present, consider hospitalization**.
Optic neuritis	E	• Stop E. • Refer patient to an ophthalmologist	• Usually reverses with cessation of E.
Arthralgias	Z FQ BDQ	• NSAIDS. • Initiate exercise regimen. • Symptoms of arthralgia generally diminish over time, even without intervention	• Uric acid levels may be elevated in patients on pyrazinamide. Allopurinol **appears not to** remediate uric acid levels.
Chest pain*	BDQ		
Chest Pain*	BDQ	• Conduct an ECG • If abnormal but <500 ms, monitor atleast weekly in consultation with a cardiologist. • If >500 ms (confirmed by repeat ECG) BDQ MUST be stopped	
Anorexia*			
Rash*			
Headache			
Blood amylase increased			

Side affect	Suspected agent(s)	Suggested management strategy	Comments
Hemoptysis			
QT prolongation	Fluoroquinolones Cfz, Bdq Possible ART causes: PIs, EFV EFV	• Any patient found to have a QTc value greater than 480 ms should be managed carefully. Check potassium, calcium, and magnesium. Electrolyte levels should be maintained in the normal range. o It is suggested to maintain potassium levels of more than 4 mEq/L and magnesium levels of more than 1.8 mg/dl. o Avoid other drugs that increase the QT interval o Monitor the patient's renal and hepatic function and adjust dose of fluoroquinolones if impairment is present. • Consider suspension of the fluoroquinolone if risk of torsades de pointes outweighs the benefits of the drug. **Comments** • The QT interval is measured from the end of the QRS complex to the beginning of the T wave on a standard electrocardiogram. • The QT is corrected for heart rate, which is referred to as the QTc and calculated by most ECG machines. • **A normal QTc is generally < 440 ms**. • Values above QTc 440 ms are referred to as prolonged. Patients with prolonged QTc are at risk for developing cardiac arrhythmias like torsades de pointes, which can be life-threatening. • Patients with QTc greater than 500 ms are at the greatest risk for developing these arrhythmias. • The fluoroquinolones cause prolongation of the QTc. • **Moxifloxacin causes the greatest QTc prolongation**, while levofloxacin and ofloxacin have a lower risk of QTc prolongation. • Currently, electrocardiogram monitoring prior to the initiation and during MDR-TB therapy is not required, as the therapeutic benefit of fluoroquinolones is considered to outweigh the risks associated with QT prolongation. • Electrocardiogram monitoring is required for patients receiving bedaquiline	• Bedaquiline should be stopped for QTc value greater than 500 ms. Consider stopping other drugs that prolong the QT interval.

Table 8.5: Recommended approaches to improving Pharmacovigillance

Monitoring for suspected drug-related problems should be part of normal patient care	• At every encounter, the responsible health-care professional should screen for any suspected ADRs. During patient investigation the possibility of a medicine-related problem should always be considered • All health-care professionals involved in patient care should be sensitized to the need to ask about and investigate adverse effects at every encounter • The forms and route for transmission of information are the same as those used in spontaneous reporting, but the forms should be supported by specific guidance (case definitions and written procedures) on when to complete them and details on standardized reporting of drug names and ADRs • The reporting may primarily target serious ADRs, rather than the notification of any suspected reaction. TSR can be adapted to the safety question at hand. If the total burden of drug-related problems in the exposed population is of interest, health professionals can be instructed to report any suspected drug-related problem. If, however, the frequency of a specific problem suspected to be associated with the therapy given is the important question, e.g. vision disorders, a case definition for reporting can be given in the instructions to health-care professionals • The reporting would last the whole length of a TB treatment episode, typically between 6 months to 2 years for a TB patient • Unlike CEM, there are no baseline measurements nor is there any active follow-up of the members of the cohort and thus fewer resources would be required • The number of TB patients in the treatment "cohort" who have been investigated would represent a denominator for calculation of simple frequencies of ADRs. • The routine patient record should include the question "Suspected adverse drug reaction? YES or NO" ensuring that the possibility has always been considered. The extent to which this information is recorded will also indicate whether ADR monitoring has become a part of normal practice. If safety monitoring of each patient is truly part of best practice and recording of whether the patient has experienced a suspected problem or not is complete, the calculated reaction frequencies may be close estimates of true incidence rates • TSR provides the opportunity to monitor every single patient on treatment, as part of treatment and care. However, implementing it would depend on the willingness of health-care providers to participate in this monitoring exercise and to report their observations. TSR will thus suffer from its voluntary nature. For the surveillance of ADRs associated with new anti-TB drugs, expected to be launched on the market in the coming years, CEM would thus be preferred over TSR.

Table 8.6: Anti-TB Drug Dosing: Adults and adolescents

Drugs	Weight Class			
	Average daily dosing	33-50kg	51-70kg	>70kg
Isoniazid (H) (100,300 MG)	10-20 mg/kg daily	200 - 300 mg daily	300mg daily or	300mg
Rifampicin ® (150, 300m mg)	10-20 mg/kg daily	450-600 mg	600 mg	600 mg
Ethambutol (E) (100, 400 mg)	25 mg/kg daily	800-1200 mg	1200-1600 mg	1600-2000 mg
Pyrazinamide (Z) (500 mg)	30-40 mg/kg daily	1000-1750 mg	1750-2000 mg	2000-2500 mg
Streptomycin (S) (1 G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Kanamycin Km (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Amikacin (AM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Capreomycin (CM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Ofloxacin (Ofx) (200,300,400mg)	The usual adult dosefor MDR-TB is 800 mg	800 mg	800 mg	800-1000 mg
Levofloxacin (LFX) (250,500 mg)	The usual adult dose for MDR-TB is 750 mg	750 mg	750 mg	750-1000 mg
Moxifloxacin (Mfx)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Gatifloxacin (Gfx) (400 mg)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Ethionamide (Eto) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Prothionamide (Pto) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Cycloserine (Cs) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Terizidone (Trd) (300 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
PAS 4gm sachets	150mg/kg daily	8gm	8gm	8-12gm

Table 8.7: Anti-TB Drug Dosing: Children

Medication	Dose	Maximum daily dose
Isoniazid(H)	10mg/kg daily	300mg
Rifampicin (R)	15mg/kg daily	600mg
Ethambutol (E)	25mg/kg daily	1200mg
Pyrazinamide (Z)	30 -40 mg/kg daily	1500mg
Streptomycin (S)	20 - 40mg/kg daily	1000mg
Kanamycin (K)	15 -30mg/kg daily	1000mg
Capreomycin (Km)	15 -30mg/kg daily	1000mg
Ofloxacin (Ofx)	15 - 20mg/kg daily	800mg
Levofloxacin (Lfx)	15 - 25mg/kg daily	1000mg
Moxifloxacin (Mfx)	7.5 -106mg/kg daily	400mg
Ethionamide (Eto)	15 – 20 mg/kg daily	1000mg
Cycloserine (Cs)	10 – 20mg/kg daily	1000mg
Terizidone(Trd)	10 – 20mg/kg daily	1000mg
Para – aminosalisylic acid (PAS)	150mg/kg daily	8g(PASER)

Table 8.8: Active Pharmacovigilance Side Effects Monitoring Tool

Intensive Phase: Monitoring done on weekly bases

MDR-TB SIDE EFFECT MONITORING FORM																																										
Intensive Phase (Adverse effect (indicate grading*)																																										
Week/Date																																										
Month of treatment																																									Management	Outcome
Date of patient review																																										
Abdominal pain																																										
Constipation																																										
Depression																																										
Diarrhea																																										
Dizziness																																										
Fatigue																																										
Fever																																										
Headache																																										
Joint pain																																										
Nausea																																										

Psychosis																																										
Rash																																										
Skin colorization																																										
Tinnitus																																										
Tremors																																										
Vision changes																																										
Vomiting																																										
Other (List)																																										
*Grading: 1 = mild; requiring no intervention	2= Moderate; requiring palliative intervention	3 = Severe; requiring change in treatment																																								
**indicate in the first column the month of treatment that treatment on intensive phase ended																																										

Table 8.9: Continuation Phase: Monitoring done on monthly bases or when indications to suspect ADRs/SE

MDR-TB SIDE EFFECT MONITORING FORM																																										
Intensive Phase (Adverse effect (indicate grading*)																																										
Monthly/Date																																										
Month of treatment																																									Management	Outcome
Date of patient review																																										
Abdominal pain																																										
Constipation																																										
Depression																																										
Diarrhea																																										
Dizziness																																										
Fatigue																																										
Fever																																										
Headache																																										
Joint pain																																										
Nausea																																										
Psychosis																																										
Rash																																										
Skin colorization																																										
Tinnitus																																										
Tremors																																										

Vision changes																																										
Vomiting																																										
Other (List)																																										
*Grading: 1 = mild; requiring no intervention												2= Moderate; requiring palliative intervention																3 = Severe; requiring change in treatment														
**indicate in the first column the month of treatment that treatment on intensive phase ended																																										

CHAPTER 9

ENGAGING COMMUNITIES, PATIENTS AND NON STATE ACTORS (NSA) IN TB, LEPROSY AND LUNG HEALTH CARE SERVICES

Background

The WHO global post- 2015 plan, endorsed at the WHO WHA in May 2014, sets the target for TB control by 2035. Among the four emphasized driving principles to end TB include: strong coalition with Non state Actors and Communities, Protection and Promotion of human rights, ethics and equity. Tuberculosis has remained a key public health challenge in Kenya. Leprosy on the other hand (though according to WHO, is at post-elimination phase), continue to affect a significant number of patients. A high percentage of patients presenting with disability grade 1&2 imply that the majority of the cases are attributed to delayed diagnosis. The deformities and disabilities often contribute to stigmatisation and/or discrimination against leprosy patients.

In order to adequately address such gaps and make further progress toward mitigating the impacts of TB, Leprosy and Lung Health, health care workers need to understand the importance of engaging communities & NSA in control of the three diseases. Increased and enhanced collaboration between Health Care workers, Communities & Non state Actors, will lead not only to improved health outcomes in TB and Leprosy (through provision of an effective continuum of care package to patient as they exist the facilities) but also an improved quality of life especially to those affected by leprosy.

Rationale and goal for engaging Community and Non state Actors in TB, Leprosy and Lung Health

- Though diagnosed in clinics and hospitals, TB and Leprosy thrives in the community. Action in the community is therefore essential in country efforts against TB and Leprosy. It is therefore important to link community action on TB and Leprosy with the work of NTLD-P so that efforts of the health systems are extended and reach as many people as possible, and also create demand for quality services.
- In order to therefore have synchronized and effective TB and leprosy patient care and support interventions, there is the need for an enhanced collaboration and coordination between the HCW and communities/NSA

The goal of engaging communities and NSA is contribute to the achievement of universal coverage and comprehensive care in TB, leprosy & Lung Health services. This goal can be realized through various strategies and activities as stipulated below

Table 9.1: Types of community engagement themes and activities

Theme	Activities
Prevention	Awareness-raising, information, education& communication, behavior change communication (BCC), infection control, training of providers
Diagnosis	Screening, contact tracing, sputum collection and transport, provider training
Referral	Linking with clinics, transport support and facilitation, accompaniment, referral forms and training of health providers
Treatment adherence support	Home based supervision and patient support, adherence counseling, stigma reduction, pill counting, training of providers, home based care and support
Social and lively hood support	Cash transfer, insurance schemes (e.g. NHIF), nutrition support and supplementation, voluntary savings and loans, inclusive market that extend choices and opportunities to the poor, training of health care providers, income generation
Stigma reduction	Community theatres/ drama groups/testimonies, partner/peer support groups, community champions, sensitizing and training facility and CHVs and leaders
Advocacy	Ensuring availability of supplies, equipments and services, training of providers, addressing governance and policies issues, working with community leaders.

Purpose

The purpose of this document is to provide simplified, stepbystep operational guidance to the community, the Ministry of Health (MOH), county government, Non state Actors (NSA), and other stakeholders in the implementation and scale-up of community TB interventions using the standardised ENGAGE-TB approach.

Target Audience

This chapter on community engagement on TB ,Leprosy and Lung disease are intended for MOH, county government, the community, and Non state Actors implementing and intending to implement TB interventions. Funding agencies and research stakeholders (especially those with interest and expertise in operational and implementation research) would also benefit from insights and directions in these guidelines to support community-based TB interventions.

Common terms and definitions

Community members are the various members of the community including but not limited to: Patients, household members, community health volunteers and community leaders

Tier 1: Community: This is the level of care in which patients seek services from the Community Health Volunteers and community Health extension workers who provide preventive, promotive and basic curative care services.

Community Unit: The community Health Unit comprise of a population of 5000 people who are served by the CHVs who range between 10-100 CHVs per community Health Unit depending on the population density. The Community Health Committee provides the required leadership at the community.

Community strategy is the mechanism through which households and communities strengthen their role in health and health related development by increasing their knowledge, skills and participation.

Community engagement: this is defined as the process of working collaboratively with and through communities to address issues affecting their well being.

Non state Actors are the public benefit organisations including: Non-Governmental Organizations (NGOs), Civil Society Organizations (CSOs), Community based Organizations (CBOs). Faith based Organizations (FBOs) and other organisations supporting the community outside the government.

Community based TB, Leprosy and Lung Health services: This refers to provision of services outside the premises of formal health facilities (e.g. hospitals, health centres, dispensaries and clinics) in community based structures (e.g. schools, places of worship, congregate settings) and homesteads.

Linkages between the Community and Facilities

Patient: The patient is at the center between the community and the health facility. Provision of holistic health care is critical in determining treatment outcome as well as quality of care for the patient.

Role of Health care workers in linking patients seen at facility level to community services:

- Ensuring that every patient referred to facility as a presumptive TB case from the community is appropriately screened for TB
- Ensuring presumptive case reaching the facility are entered into the presumptive/ contact investigation register(where applicable)
- Probing for person referring the presumptive case to the facility especially those referred by CHVs
- Ensure active contact investigation of all cases who turn positive for the disease (TB, Leprosy).

- Assisting all patients to identify appropriate treatment supporters to ensure adherence.
- Linking patient to community or programs for support
- Referring patient vertically or horizontally.

Community based approaches

A. **The basic approaches for case identification and diagnosis:**

- Identification of people with signs and symptoms of TB, Leprosy and Lung disease using community screening tool(intensive case finding)
- Referral of presumptive TB, Leprosy cases to facility for further evaluation
- Collection and shipment of sputum's to facilities(where applicable)
- Contact tracing (use of facility TB/Leprosy data to follow up on contacts of bacteria logically confirmed TB patients; multibacillary leprosy patients)

B. **The basic approaches for patient care and support include:**

1. Implementation of good DOTS program at community level.
   a. Advice patient on availability of community based patient management option (ambulatory services) for both drug sensitive and resistant TB and leprosy management
   b. Provision of DOT for Rifampicin based regimens at household level.
2. Promote provision of social and livelihood support (Social protection for TB, leprosy patients including but not limited to:
   - Nutrition support,
   - Income-generation activities for the aged, orphaned and vulnerable children etc.).
   - Stipends/NHIF
3. Refer / link patients for Psycho-social support (to existing community based program providing care and support services including
   - Counseling
   - Patient follow up to ensure completion of treatment
     - Home visits by community health volunteers to ensure adherence to medication and nutritional therapy
     - Tracing of patients who might interrupt treatment
4. Link and or refer leprosy patient (those with disability grade 1&2) for rehabilitative services (social, surgical etc).

C. **The basic approach for infection control at the community level:**

- Health education of the patient, family and community on how to minimize disease transmission at household level

- Vaccination of children with BCG. BCG vaccination at birth or in the first year of life provides proven partial protection against leprosy. Organizations should actively encourage government health services to maintain a high coverage.
- Promote provision of IPT for children exposed to infectious cases.

N/B For purposes of continuum of care, reverse referral or up down from facility to community is applied e.g. for home based care services.

Roles of various community stakeholders in TB, Leprosy & Lung Health disease control activities

1. **TB Treatment Supporters**
    - Provision of DOT (Directly Observed Treatment) to ensure compliance and adherence of treatment
    - Provide psychosocial support e.g. counseling etc
    - Provide food and nutritional support
    - Follow up if any problems occur or if the patient does not adhere to treatment schedules.
    - Ensure regular refill/replenishment of drugs
    - Ensure medicines are stored in a dry and cool place (away from heat and direct sunlight) in the house and away from children.

2. **Community Health Volunteers (CHV)**
    1. Create awareness on TB, Leprosy & Lung Health and available services to the community
    2. Identify, screen, and refer presumptive TB/leprosy clients to health facility and follow up on the outcome
    3. Support patients on treatment and adherence
    4. Tracing of treatment interrupters and patient contacts
    5. Refer TB patients on treatment for follow-up sputum smears
    6. Record and report information using the standard tools
    7. Identify complications, including adverse drug reactions, and refer as needed
    8. Participate in periodic review meetings organized by the CHEW
    9. Promote infection prevention and control interventions at Household/ community level
    10. Link patients to support groups
    11. Perform nutrition assessment using mid-upper-arm circumference (MUAC) and refer appropriately

Note: *These activities are achieved mainly through home visits, barazas, etc.*

3. **Community Health Extension Workers (CHEWs)**

Community Based CHEWs (directly in contact with CHVs/Community Health Committee (CHC)

1. Oversee the identification of community health Volunteers (CHVs).
2. Plan and build the capacity of CHVs.
3. Sensitize the CHVs on side effects monitoring (pharmacovigilance)
4. Monitor the management of TB, Leprosy patients in the community.
5. Generate and collate data for decision making.
6. Link community and the health facility for action
7. Organize community health activities including dialogue days and health action days
8. Organize periodic review meetings with the CHVs.
9. Organize and conduct school health activities (TB, Leprosy, Lung Health)
10. Provide support supervision to CHVs
11. Ensure patients are appropriately notified and monitored at the community
12. Receives reports from the CHC / CHV and forward to HRIO
13. Coordinate/Link community based interventions with Non state Actors

Facility based CHEW

1. Oversee the identification of community health Volunteers (CHVs)
2. Plan and build the capacity of CHVs.
3. Sensitize the CHVs on side effects monitoring (pharmacovigilance)
4. Organize health outreach service in collaboration with community based CHEW
5. Monitor the management of TB, leprosy patients in the Facility
6. Generate and collate data for decision making.
7. Link community and the health facility for action
8. Organize periodic review meetings with the CHVs.
9. Initiate referrals of patients and clients to the community
10. Generate community reports and forward to sub county HRIO/ TB coordinator

Health care workers

1. Conduct CMEs within their facilities on TB, Leprosy and Lung Health
2. Screening of presumptive cases (TB, Leprosy,)patients
3. Identification of patients interrupting treatment and notifying the CHEW
4. Health educate patients diagnosed with TB, Leprosy and Lung disease
5. Monitoring Patients for side effects and reporting accordingly (pharmacovigilance)
6. Monitor the management of TB, leprosy patients in the community,
7. Ensure proper documentation in the TB/Leprosy tools.
8. Generate and collate data for decision making.
9. Link community and the health facility for action

10. Organize periodic review meetings with the CHVs.
11. Provide support supervision to CHVs
12. Ensure patients are appropriately notified and monitored

Non state Actors (NSA)

- Empower communities to participate in matters relating to their own health
- Mobilize communities to participate in resource mobilization for their livelihood
- Advocate for budget allocation and mobilize resources for sustainable community interventions.
- Influence other stakeholders to embrace TB/ leprosy in their day to day activities.
- Support and participate in the implementation of TB, leprosy control activities
- Promote behavior change through various channels of communication to reduce stigma and discrimination.
- Identify and work with Key populations
- Facilitate implementation of Intensive Case Finding (Screening, referral and testing)
- Support and participate in home based care activities.
- Promote treatment adherence through peer support groups, education, and individual follow-up.
- Promote provision of social and livelihood support to TB, leprosy patients (e.g. stipends/ food support, income-generation activities for the aged, orphaned and vulnerable children etc.).
- Promote patients' rights and responsibilities.
- Promote infection prevention and control interventions at community level.

Note: Information on how to effectively engage Non state Actors / CSOs in TB control activities can be found in the ENGAGE TB guideline.

Monitoring community engagement

WHO has developed a minimum set of standardized indicators to help monitor contributions made by communities (particularly CHVs) whether supported by government or by partners.

Indicators:

1. Number and % of new patients with TB (all forms) diagnosed and notified who were referred by CHVs
2. Number and % of new patients with TB (all forms)successfully treated (cure plus completed treatment)who received support for treatment adherence from CHVs

Other indicators

3. Number and % of treatment defaulters traced by CHVs
4. Number of presumptive TB cases referred by CHVs to facilities for screening
5. Number and % of contacts traced and referred by CHVs to facilities for screening for TB

Patients' Rights and Responsibilities (Patients' Charter)

The Patients' Charter for Tuberculosis Care (The Charter) outlines the rights and responsibilities of people with TB. It empowers people with the disease and their communities through this knowledge. Initiated and developed by patients from around the world, *The Charter* makes the relationship with health care provider's mutually beneficial one.

The Charter sets out the ways in which patients, the community, health providers (both private and public), and governments can work as partners in a positive and open relationship with a view to improving TB care and enhancing the effectiveness of the health care process. It allows for all parties to be held more accountable to each other, fostering mutual interaction and a "positive partnership."

The Patients' Charter for Tuberculosis Care practices the principle of Greater Involvement of People with Tuberculosis (GIPT). This affirms that the empowerment of people with the disease is the catalyst for effective collaboration with health providers and authorities and is essential to victory in the fight to stop TB. *The Charter*, the first global "patient-powered" standard for care, is a cooperative tool, forged from a common cause, for the entire TB community

Patients' Rights

You have the right to:

Care

- The right to free and equitable access to TB care, from diagnosis through treatment completion, regardless of resources, race, gender, age, language, legal status, religious beliefs, sexual orientation, culture, or having another illness.
- The right to receive medical advice and treatment which fully meets the new International Standards for Tuberculosis Care, centering on patient needs, including those with MDR-TB or TB-human immunodeficiency virus (HIV) co-infections and preventative treatment for young children and others considered to be at high risk.
- The right to benefit from proactive health-sector community outreach, education, and prevention campaigns as part of comprehensive care programmes.

Justice

- The right to make a complaint through channels provided for this purpose by the health authority and to have any complaint dealt with promptly and fairly.
- The right to appeal to a higher authority if the above is not respected and to be informed in writing of the outcome.

Organisation

- The right to join, or to establish, organisations of people with or affected by TB and to seek support for the development of these clubs and community-based associations through the health providers, authorities, and civil society.
- The right to participate as "stakeholders" in the development, implementation, monitoring, and evaluation of TB policies and programmes with local, national, and international health authorities.

Dignity

- The right to be treated with respect and dignity, including the delivery of services without stigma, prejudice, or discrimination by health providers and authorities.
- The right to quality health care in a dignified environment, with moral support from family, friends, and the community.

Information

- The right to information about available health care services for TB and what responsibilities, engagements, and direct or indirect costs are involved.
- The right to receive a timely, concise, and clear description of the medical condition, with diagnosis, prognosis (an opinion as to the likely future course of the illness), and treatment proposed, with communication of common risks and appropriate alternatives.
- The right to know the names and dosages of any medication or intervention to be prescribed, its normal actions and potential side-effects, and its possible impact on other conditions or treatments.
- The right of access to medical information which relates to the patient's condition and treatment and to a copy of the medical record if requested by the patient or a person authorised by the patient.
- The right to meet, share experiences with peers and other patients, and to receive voluntary counseling at any time from diagnosis through treatment completion.

Choice

- The right to a second medical opinion, with access to previous medical records.
- The right to accept or refuse surgical interventions if chemotherapy is possible and to be informed of the likely medical and statutory consequences within the context of a communicable disease.
- The right to choose whether or not to take part in research programmes without compromising care.
- The right to job security after diagnosis or appropriate rehabilitation upon completion of treatment.
- The right to nutritional security or food supplements if needed to meet treatment requirements.

Patients' Responsibilities

You have the responsibility to:

Share Information

- The responsibility to provide the health care giver with as much information as possible about present health, past illnesses, any allergies, and any other relevant details.
- The responsibility to provide information to the health provider about contacts with immediate family, friends, and others who may be vulnerable to TB or may have been infected by contact.

Follow Treatment

- The responsibility to follow the prescribed and agreed treatment plan and to conscientiously comply with the instructions given to protect the patient's health, and that of others.
- The responsibility to inform the health provider of any difficulties or problems with following treatment or if any part of the treatment is not clearly understood.

Contribute to Community Health

- The responsibility to contribute to community well-being by encouraging others to seek medical advice if they exhibit the symptoms of TB.
- The responsibility to show consideration for the rights of other patients and health care providers, understanding that this is the dignified basis and respectful foundation of the TB community.

Confidence

- The right to have personal privacy, dignity, religious beliefs, and culture respected.
- The right to have information relating to the medical condition kept confidential and released to other authorities contingent upon the patient's consent.

Show Solidarity

- The moral responsibility of showing solidarity with other patients, marching together towards cure.
- The moral responsibility to share information and knowledge gained during treatment and to pass this expertise to others in the community, making empowerment contagious.
- The moral responsibility to join in efforts to make the community TB-free

ENGAGE-TB Approach

1. The ENGAGE-TB approach seeks to shift the global perspective of TB from a medical illness to a more comprehensive socio-economic and community problem. ENGAGE-TB is a brand that suggests six key areas to facilitate the engagement of NON STATE ACTORSs in TB and TB/HIV interventions. These are
    a. Situation analysis
    b. Enabling legal and policy environment
    c. Guidelines and tools
    d. Assessing the relevant TB tasks needed to be undertaken and included in action plans
    e. Monitoring and evaluation to enable learning
    f. Continuous improvement and enhancing of the capacity of organizations in order for them to scale up their work in a sustainable way

The ENGAGE-TB Approach Components

- **Situation analysis**
- **Enabling environment**
- **Guidelines and tools**
- **TB task identification**
- **Monitoring and evaluation**
- **Capacity-building**

The ENGAGE-TB approach emphasizes the value of collaboration and partnership between NON STATE ACTORSs, the TB programme, and other partners. ENGAGE-TB recommends close alignment of systems, especially in TB monitoring and reporting, to ensure national data adequately captures the contributions of NON STATE ACTORSs in TB activities.

Integrating TB Activities

NGOs and other NON STATE ACTORSs could integrate TB into their community-based work in many ways, without trained medical staff. It is particularly important for them to do so when they are working with high-risk populations (such as people living with HIV and the very poor), people living in congested environments (urban slums and prisons), people who use drugs, sex workers, and migrant workers.

TB activities that can be integrated in the community

Assisting Early Case Finding

Encourage people who present with symptoms of TB such as chronic cough, weight loss, night sweats, and fever to contact a health worker or visit a health facility. Sputum examination is the mainstay of TB investigation in many settings. In community meetings (e.g., women's groups, health clubs, farmers' groups), the main symptoms of TB could be explained. People with symptoms could be helped to have their sputum examined by transporting either the person or the sputum sample to the nearest health facility.

Providing Treatment Support

Patients being treated for TB may require support to take their drugs and finish their treatment. Family members and community-based volunteers and workers can be trained as treatment supporters by NGOs and other NON STATE ACTORSs. Patients can also be provided with nutritional and psychosocial support, if needed.

Preventing the Transmission of TB (IPC)

Covering the mouth and nose when coughing and sneezing is a simple behaviour change that can help to limit the spread of infected sputum particles and so reduce the risk to others of being infected. NGOs and other Non state Actors(NSA) could spread this message using their various social-communication media.

HIV Programmes and Projects

Encouraging every person living with HIV to be screened for TB and, depending on the result, helping them receive TB prevention treatment (isoniazid preventive therapy) or further examination for TB disease.

Maternal and Child Health Programmes and Projects

Encouraging all pregnant women to test for HIV and to be screened for TB symptoms at the nearest facility. Children under five are particularly vulnerable to TB infection if an adult in the home has TB. Health workers should be made aware of this and keep watch for any symptoms and signs of TB in households with young children.

Education Programmes and Projects

Incorporating messages of TB prevention and care into curricula and classroom learning. Schoolchildren should be able to recognize TB symptoms and the importance of sputum examination so that they can encourage those at home who might have TB to get tested.

Agriculture and Income-Generation Programmes and Projects

Raising awareness about TB symptoms and signs amongst organised groups (such as farmers' groups and savings and credit groups). Members with symptoms of TB could be encouraged to get their sputum examined. Those being treated for TB could be supported to complete their course of treatment. Nutritional and psychosocial support will improve the outcome of TB treatment.

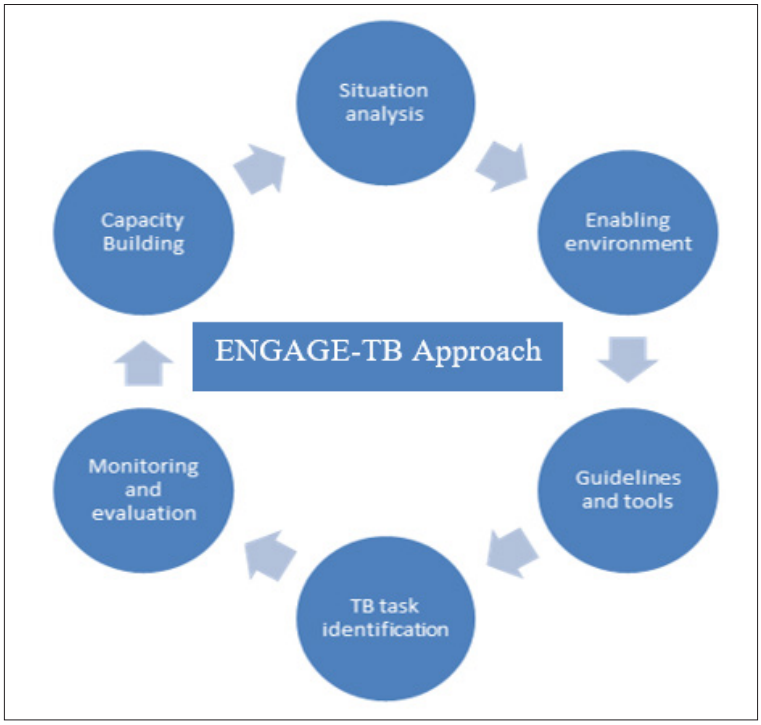
The principles of ENGAGE-TB are:

1. Mutual understanding and respect.
2. Consideration for local contexts and values.
3. A single national system for monitoring with standardised indicators.

Components of ENGAGE-TB approach

The six components of the ENGAGE-TB approach are as follows:

Figure 9.1: The ENGAGE-TB Approach Framework



Situation Analysis

The situation analysis is a key component that will help to identify the specific needs and tasks that will be undertaken for integrated, community-based TB activities. It involves information gathering at all levels by the different actors to analyse and understand the existing situation. It is useful to involve and engage multiple stakeholders including the MOH, county governments, NON STATE ACTORSs, and community members.

The situational analysis should identify and prioritise key problem situations and needs in TB prevention and care activities. Existing opportunities and key stakeholders in TB activities, including in community-based TB activities, should be identified to forge synergies, use resources efficiently, and prevent duplication of efforts. Particular emphasis should be given to identifying effective community structures that are best positioned to address the problems and gaps identified in the situation analysis. Information on the available TB diagnostic and treatment facilities provides an understanding of how the system will work in terms of concrete activities such as referral, sputum collection, diagnosis, treatment, and follow-up. In situations where capacity is limited, alternate mechanisms to ensure high-quality service delivery, including adequate supply of anti-TB drugs and diagnostics, should be identified in accordance with the national policies and guidelines. The situation analysis should also look into other critical areas such as incentives that can be used to improve the performance of community-based TB and TB/HIV activities based on the local context.

Areas for review during situation analysis

- Document the overall TB situation in the country and / or areas of intervention (NTP).
- Map the most-at-risk populations for TB in the operational area.
- Availability of high-quality TB diagnosis and treatment capacity (e.g., laboratory and drugs) and any existing gaps.
- Mapping of the existing health care facilities (public, private).
- Other key players implementing community-based TB and TB/HIV care activities.
- Document the best existing community-based structures for community-based TB and TB/HIV activities.
- Existing capacity of the NGO/NONE STAE ACTORSs to use the structures for community-based TB and TB/HIV activities.
- Identify the strengths, weaknesses, opportunities, and threats of TB and TB/HIV control interventions.
- Document the existing key barriers for delivery of TB and TB/HIV services.
- Propose the critical areas that need collaboration between NGOs/NONE STAE ACTORSs and the NTP.
- Document the existing linkages between the NONE STAE ACTORSs and the TB programme.
- Document the existing indicators currently in use by the NONE STAE ACTORSs/ community groups on TB.

Both qualitative and quantitative methods can be used to gather information and improve understanding of the situation.

Enabling Environment

A mutually enabling legal and policy environment based on principles of equity, equality, and mutual respect will greatly help to support the increased engagement of NON STATE ACTORSs in TB activities. This is particularly true for NON STATE ACTORSs who are newly engaged with TB prevention and care activities. Reducing the complexity of transactions and increasing the speed of facilitation are key to improving the operating environment for NON STATE ACTORSs. The TB programme has the responsibility of creating an enabling policy environment to facilitate effective engagement of NON STATE ACTORSs in TB prevention, diagnosis, treatment, and care services. This should be done in close consultation with all relevant stakeholders involved in TB control. NON STATE ACTORSs also have to play a proactive role to stimulate and support the development of an enabling policy environment through constructive dialogue and engagement with the TB programme, and with full participation of the national coordinating body (NCB) that has been formed to represent NON STATE ACTORSs' best interests and also help to systematically share and disseminate lessons learnt by individual member organisations.

Examples of areas that need to be agreed between CSOs and the NTP
Defining roles and responsibilities of different actors.
Developing national policy and operational guidelines.
Agreeing on national plans and targets.
Establishing a code of conduct to promote accountability.

At the community level, the NON STATE ACTORSs, especially the local NGOs, NON STATE ACTORSs, and FBOs should support the growth and development of NON STATE ACTORSs that include TB prevention, care, and support in their mission. Existing NON STATE ACTORSs, such as HIV support groups, could also be approached to integrate TB in their work (and TB groups should be encouraged to integrate HIV support). It will be important for NON STATE ACTORSs to create mechanisms to interact regularly with these NON STATE ACTORSs, listen and respond to their concerns, and promote their continuing growth and empowerment.

The following are key points for consideration:

The NCB should be functional at all administrative levels (national, county, and local) to facilitate the effective engagement of NON STATE ACTORSs in community-based TB prevention, diagnosis, treatment, and care services. NCB is tasked with the following activities:

1. *Coordinating and organizing regular meetings.*
2. *Engaging new NON STATE ACTORSs in TB health care activities.*
3. *Participating in review of TB policy guidelines.*
4. *Developing code of conduct to be followed by all participating members.*

- *The NCB has derived representation from patients and affected communities, including new and existing NON STATE ACTORSs in TB control interventions. The NCB shall have regular meetings and will develop mechanisms for information-sharing and discussing concerns and issues of common interest relating to community-based TB activities and the relationship with the TB programme.*

- *The NCB representatives should ensure that all NCB members are fully involved in ongoing discussions and negotiations and have the opportunity to provide input and receive feedback regularly.*
- *The more developed NON STATE ACTORSs and international organisations not directly dealing with TB intervention should be approached to support the growth and development of NON STATE ACTORSs active in TB prevention, care, and support. The new players will receive the information and training they need as well as financial support for their expenses. Their links to formal health care facilities should be strengthened and their access to diagnostic and treatment facilities improved. Their efforts to reach out to members of their own communities should be supported.*

- *The NCB and National TB Programme agreed on a code of conduct that clarifies roles, responsibilities, and decision-making processes, defining acceptable professional behaviors, and providing benchmarks for evaluation and reporting.*

Guidelines and Tools

The MOH and partners are working with NON STATE ACTORSs and community representatives in the NCB to jointly review and make available national operational guidelines and standard tools.

Examples of tools

- **National operational guidelines for CSOs on TB prevention and management.**
- **National curriculum for training of health workers including CHVs and DOTS supporters.**
- **Code of conduct guide formalising the relationship between CSOs/ partners and the MOH.**
- **M&E framework on CSOs and community engagement.**

TB Task Identification

The current Stop TB Strategy and its components provide the basic framework for the key TB tasks that need to be implemented in the prevention, diagnosis, treatment, and care of TB (drug-sensitive, drug-resistant, and HIV-associated TB). To increase synergy and effectiveness in joint planning for these key tasks, it is important that all parties involved (including NON STATE ACTORSs) assess the tasks to be carried out.

TB is closely linked with HIV and is closely related to social determinants such as poverty, crowding, drug and alcohol use, and non-communicable diseases such as malnutrition, and diabetes mellitus. Therefore, the task identification needs to consider the opportunities, capacities, and comparative advantages of the NON STATE ACTORSs working in such areas and decide how best to address TB.

Tasks for CSOs and other stakeholders engaged in TB-control activities

- Awareness creation and raising demand-generation for services.
- Behaviour change communication for community mobilisation.
- Stigma reduction.
- Advocacy at all levels (e.g., for improved availability of services and drugs).
- Active community-based TB case finding (e.g., through campaigns or house-to-house visits).
- Sputum collection and transport.
- Tracing of contacts with infectious TB cases in their families and communities.
- TB treatment adherence support.
- Promote use of Patient's Charter for TB Care.
- Screening, prophylaxis, and treatment of TB for people living with HIV.
- HIV testing and counseling for TB patients.
- Management of patients with MDR and XDR TB.
- TB prevention and care at individual, household, and community levels.
- Information-sharing and networking to address social determinants of health and social protection.
- Support to improve the health care delivery system (e.g., human resource, infrastructure, supply).
- Conduct programme-based operational research.
- Financing and resource mobilisation.

Furthermore, consideration must be given to the availability of resources and expert ways and means to secure synergies. The TB programme has included the implementation and scaling up of community-based TB activities in the national TB strategic plans. The action plans can be stand-alone for addressing TB or integrated into broader action plans (e.g., inclusion into existing HIV, maternal, and child health). NON STATE ACTORSs implementing TB prevention and care services should include community-based TB activities in their strategic plans. NON STATE ACTORSs working on health issues that are intricately linked with TB (e.g., HIV, MCH, non-communicable diseases such as diabetes mellitus, tobacco, drug use, and alcoholism) should include TB prevention, diagnosis, treatment, and care and integrate these into their activities.

The following are key points for consideration:

- *Joint consultation between NON STATE ACTORSs and MOH is recommended when assessing and determining the tasks for implementation.*
- *The plans should address the key gaps identified in the situational analysis and include key TB tasks.*

- *SMART (specific, measurable, achievable, realistic, time-bound) objectives should be framed around the main tasks identified in the process.*
- *TB patients' representatives should be involved in the development and implementation of the strategic plan.*
- *Particular emphasis must be placed on ensuring that the planned activities are aligned with national policies and guidelines.*

Monitoring and Evaluation

Regular monitoring and evaluation will help to assess the quality, effectiveness, coverage, and delivery of community-based TB activities through the engagement of NON STATE ACTORSs. It promotes a learning culture and serves as a foundation to ensure continuous improvement of programme implementation. The MOH should ensure that there is one strong national monitoring and evaluation system that recognises the contribution and engagement of NON STATE ACTORSs. Electronic systems and modern technologies should be explored, standardised, and used to improve the monitoring and evaluation system.

Examples of areas for learning and follow-up

- **Choice of target groups and ability to reach these.**
- **Appropriateness of initial targets set and need for revision.**
- **Bottlenecks in case detection/referrals/treatment care and support.**
- **Difficulties faced by patients and their communities in securing services.**
- **Difficulties in the arrangements between CSOs and the NTP.**
- **Scaling-up of best practises.**

Quarterly reviews of progress would help to uncover issues in implementation and enable mid-stream correction to plans and budgets and to overall strategy. The MOH should help to smooth any operational difficulties NON STATE ACTORSs may face and cannot independently resolve. Quarterly meetings to discuss the review findings could be held at regional or local levels so that there is cohesion of learning between NON STATE ACTORSs and with the MOH. Annual meetings at the national level should be coordinated by the NCB and a broad spectrum of implementing NON STATE ACTORSs invited to share their review findings and progress reports. The ensuing national report should be shared widely with all stakeholders within government, NON STATE ACTORSs, patients and community members, donors, and the general public.

Evaluation of the results of the initial implementation of the action plan is important to guide further expansion and scale-up of the activities by the NON STATE ACTORSs. The evaluation should be an ongoing process and include evaluation of both the activities (process evaluation) and the achievement of the objectives (impact evaluation) of the action plan.

The following are key points for consideration:

- *The MOH, in consultation with the NCB, should develop a set of nationally recommended and standardised data-collection and reporting tools aligned to the national TB strategies for use by NON STATE ACTORSs.*
- *Develop a set of nationally agreed indicators jointly with NON STATE ACTORSs to measure the effective engagement of NON STATE ACTORSs and their implementation of community-based TB activities.*
- *Enhance the standardised use of electronic systems and processes in the monitoring and evaluation of community-based TB activities.*
- *Establish mechanisms that enable patients, clients, and their affected communities to contribute to the monitoring of the implementation of community-based TB activities to increase accountability, responsiveness, and the quality of services.*
- *The NCB develops standardised tools of supportive supervision to enable its members to better monitor community-based TB and TB/HIV activities that are aligned with national policies and guidelines.*
- *National surveillance and reporting systems should explicitly reflect the contributions of NON STATE ACTORSs. The reports should also be enriched by their perspectives on the data and analyses, as secured via meetings of the National TB and TB/HIV Coordinating Body.*
- *Each implementing agency should undertake a full evaluation at least once every five years. The MOH should support a national evaluation process every five years, using the results from various implementing partners, through a participatory and consultative process that includes all stakeholders and using existing opportunities such as National TB Programme Reviews.*
- *The outcomes of periodic evaluations should be communicated widely, especially with the MOH, NCB, patients, community members, and local policymakers to share learning and also to use findings for advocacy.*

Capacity-Building

Capacity-building is critical to strengthen and sustain the engagement of NTP and NON STATE ACTORSs in implementing and scaling up community-based TB activities. It requires joint actions by the NON STATE ACTORSs and will be of mutual benefit to them. Capacity-building needs and approaches can vary between regions and settings, depending on factors such as the local environment for engagement of NON STATE ACTORSs, and the type of health system to support the implementation of community-based TB and TB/HIV activities.

Increasing financial capacity through increased availability of resources is crucial for scaling up community-based TB and TB/HIV activities and the effective engagement of NON STATE ACTORSs. Innovative means of resource mobilisation from internal (e.g., national governments, private donations, philanthropy) and external sources (e.g., the Global Fund to Fight AIDS, TB, and Malaria, bilateral donors and charitable foundations) should be sought both by NON STATE ACTORSs and the NTP. Operational research is another key area in which the MOH and NON STATE ACTORSs with research expertise (e.g., professional associations) should collaborate to improve the performance and implementation of the programme.[1]

Capacity-building interventions should also support sharing and transfer of knowledge, skills, and resources between international NON STATE ACTORSs and indigenous NON STATE ACTORSs, with both sets of organisations gaining from the process. Regular forums for sharing knowledge, experience, and good practises amongst members should be established. With such mutual learning and support, confidence and capability can grow and enable the scaling-up of activities.

Examples of capacity-building areas

- **Human resources – expanding the number of employees and DOTS supporters available and also their knowledge and skills in the fields to which they are deployed.**
- **Financial resources – increasing the ability to attract and retain additional funding for such initiatives from a wide range of multilateral, bilateral, institutional and private donors.**
- **Physical resources – enabling the investments needed in assets such as vehicles, computers, and facilities that allow organisations to scale up activities.**
- **Management and leadership development – improving management capacity within organisations and improving governance and leadership to ensure growth is accompanied by increasing accountability and transparency.**
- **Systems development and strengthening.**

The following are key points for consideration for each organisation:

- *Conduct needs assessment to identify capacity-building needs in order to implement and scale up community-based TB and TB/HIV activities.*
- *The needs assessment should cover a broad range of areas, including capacity in health service delivery, quality and adequacy of the health workforce, including CHVs and DOTS supporters, monitoring and evaluation, training, advocacy, operational research, and organisational development.*
- *Ensure that specific capacity-building measures, based on the assessed gaps, are woven into the annual plans of each organisation so that there is systematic progress in improving capacity.*
- *The NCB, in consultation with the MOH, should develop a standardised training curriculum for community-based TB activities to be used by NON STATE ACTORSs, which should be adaptable to their mission, organisational structure, and comparative advantage.*
- *NON STATE ACTORSs should ensure that their staff are trained, especially on the instruments needed for monitoring and evaluation. Where needed, the MOH should provide support for such training.*
- *International NGOs working in partnership with indigenous NON STATE ACTORSs should work to transfer financial resources, knowledge, and skills to support identified capacity gaps and so build local capacity to scale up community-based TB and TB/HIV*

activities. Training and support in fundraising will also be required to sustain indigenous NGOs and NON STATE ACTORSs after their INGO partnership ends.

- *Indigenous NON STATE ACTORSs should similarly share their knowledge and skills and understanding of local realities with international NGOs to enrich their plans and ability to have positive impact.*
- *The NCB, at all levels, should support processes that allow learning to be transferred from one member to the other and can also become available to new entrants to community-based TB and TB/HIV activities. Tools that have been developed and lessons that have been learnt should be widely shared and be made available.*

Governance at the Community Level

Definition of Governance

Governance relates to decisions that define expectations, grant power bestowed by the Community Health Committee (CHC) constitution, or verify performance. It consists of either a separate process or as part of management or leadership processes. Governance implies the practise of decision-making in ways that are transparent and fair/honest. Through this process, the interests of local communities are protected.

Importance of Good Governance

The presence of good governance practises at the community level clarifies authority, simplifies decision-making, and ensures leaders and institutions are accountable for their actions and decisions. Good governance does the following:

1. Promotes trust in the institutions and the community.
2. Enhances services to the community and stakeholders.
3. Improves decision-making and the quality of these decisions.
4. Connects institutions to the community and stakeholders.
5. Enhances the perception of the institutions amongst community members and stakeholders.
6. Improves the ability to weather a crisis.
7. Improves financial stability.

Principles of Good Governance

Good governance assures that corruption is minimised, the views of minorities and marginalised groups are taken into account, and that the voices of the most vulnerable in society are heard in decision-making. It is also responsive to the present and future needs of community.

Participation

Participation by both men and women is a key cornerstone of good governance. Participation at community level could be through legitimate intermediate representatives (the CHC members representing the community).

It is important to point out that representatives shall strive to ensure that the concerns of the most vulnerable in the community would be taken into consideration in decision-making. Participation needs to be informed and organised.

Transparency

Transparency means that decisions taken as well as their enforcement are done in a manner that follows guidelines and regulations. It also means that information is freely available and directly accessible to those who will be affected by such decisions and their enforcement. It also means that enough information is provided and that it is provided in easily understandable forms and media.

Responsiveness

Good governance requires that institutions and processes try to serve all community members and stakeholders.

Consensus-Oriented

There are several actors and as many viewpoints in a given society. Good governance requires mediation of the different interests to reach a broad consensus on what is in the best interest of the whole community and how this can be achieved. It also requires a broad and long-term perspective on what is needed for sustainable community health outcomes and how to achieve the goals of such development. This can only result from an understanding of the historical, cultural, and social contexts of a given community.

Equity and Inclusiveness

A community's well-being depends on ensuring that all of its members feel that they have a stake in it and do not feel excluded from the mainstream. This requires that all groups, but particularly the most vulnerable, have opportunities to improve or maintain their well-being.

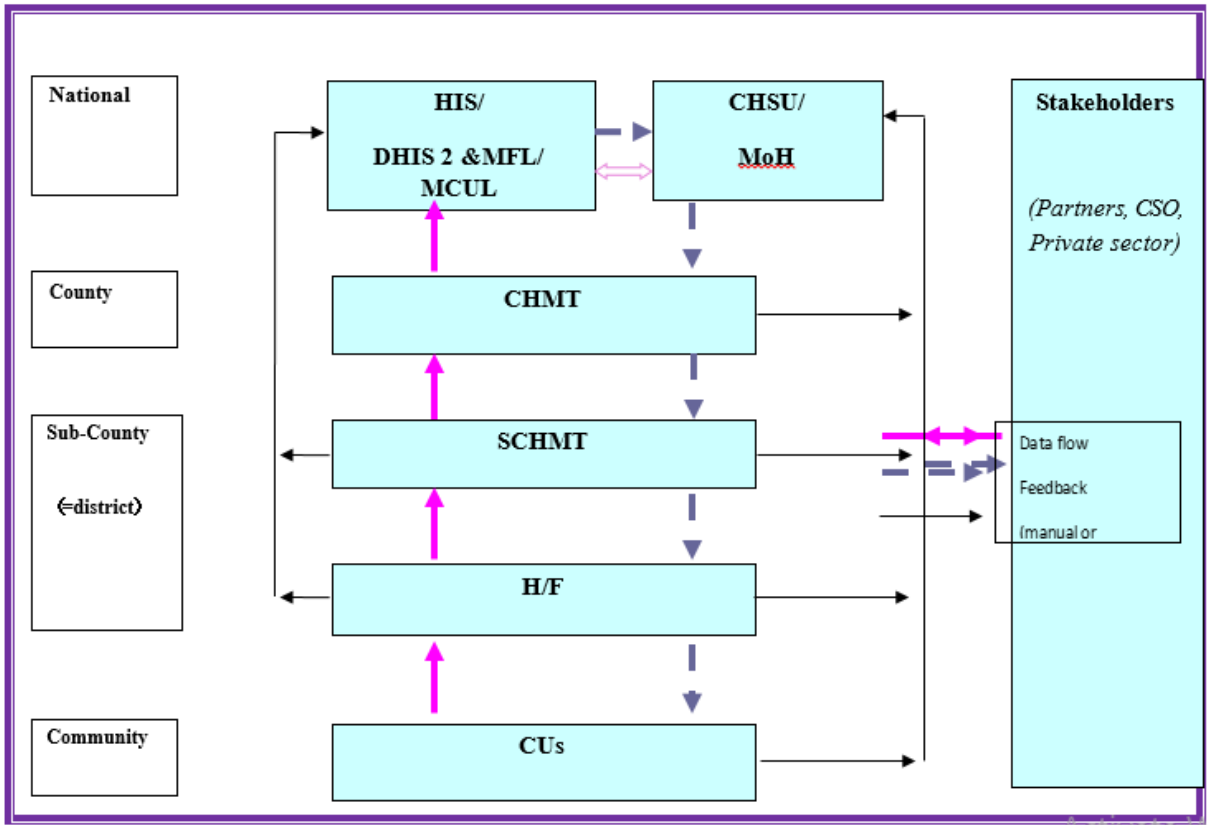
Effectiveness and Efficiency

Good governance means that processes and institutions produce results that meet the needs of the community whilst making the best use of resources at their disposal. The concept of efficiency in the context of good governance also covers the sustainable use of natural resources and the protection of the environment.

Accountability

Accountability is a key requirement of good governance. Not only governmental institutions, but also community-Non-state actorsbased organisations must be accountable to the community they serve and to their institutional stakeholders.

Figure 9.2: Organogram/Data and information flow



TB Case Management at the Community Level

Definition of TB

TB is a chronic infectious disease; it is caused by a bacillus (bacteria) known as Mycobacterium tuberculosis. TB mostly affects the lungs, though other parts of the body can be affected, except for teeth, hair, and nails.

Types of TB

There are two types of TB, depending on the part of the body affected:

- Pulmonary, which affects the lung (smear-positive and smear-negative).
- Extra-pulmonary, which affects other parts of the body.

Mode of Transmission

TB is spread through air by droplets from a person with TB disease to a healthy person. The droplets are generated through coughing, sneezing, talking, singing, and laughing.

Risk Factors

Risk factors are factors that may contribute to TB infection, transmission, and development of TB disease (both social and biological determinants).

The following are the key risk factors for TB:

- Malnutrition.
- Chronic diseases (e.g., diabetes).
- Immunosuppressive drugs (e.g., cancer drugs).
- Age (there is increased susceptibility in the very young and very old).
- HIV infection.
- Poor ventilation and poor lighting.
- Unhygienic cough.
- Overcrowding.
- Poverty.
- Low social-economic status.
- Occupational exposure (e.g., asbestos, silica mines, households emitting high particulate matters such as biofuel smoke).
- Chronic alcoholism/smoking.

Signs and Symptoms of TB

- Cough lasting two weeks or more.
- Chest pain.
- Fever.
- Night sweats.
- Loss of appetite.
- Weight loss.
- Blood in the sputum.
- For extra-pulmonary TB, the patient may notice the following signs and symptoms, amongst others:
    - Painless enlarged lymph nodes.
    - Oozing matted lymph nodes (lymph nodes that are discharging pus).
    - Breathlessness and fatigue.

Diagnosis of TB

- History of patients and/or of family members with TB.
- Physical examinations.
- Laboratory (sputum, biopsy, etc.) examination.
- X-ray (chest, bones, etc.) in some instances.

Diagnosis of TB in Children

- Cough of two or more weeks.
- History of contact with active TB.
- Unexplained fever.
- Failure to thrive (poor growth).
- Weight loss.

Importance of Sputum Examination

- Confirm the diagnosis.
- Monitor the patient's response to treatment.
- Determine treatment outcome(s) and declare if the patient is cured or not.

NOTE: Sputum is collected twice, immediately when requested (spot) followed by an early morning specimen.

Factors That May Affect Early Diagnosis of TB

- Cost (pre-diagnosis).
- Distance to the health centre.
- Patient's preference for traditional healers and prayers before seeking treatment.
- Barriers in communication between health workers and clients.
- Ignorance of the facts on TB.
- Stigma.

Other Diagnostic Key Points to Note

If smears are negative, other modern diagnostic tools for investigations could be considered, which include:

- Chest x-ray.
- GeneXpert®.
- Culture and DST.

Treatment - Case Holding and Follow-Up

Aims of TB Treatment:

- To cure patients of TB.
- To prevent death from TB.
- To decrease TB transmission.
- To reduce TB recurrence/relapse.
- To prevent drug-resistant TB.

TB Treatment

New TB Case

TB treatment comprises two phases: 1) Intensive phase of two months (Rifampicin, isoniazid, Pyrazinzmid and Ethambutol); 2) Continuation phase of four months (Rifampicin and isoniazid).

Re-Treatment

This also comprises two phases. First is the intensive phase, which comprises two months of streptomycin injection plus Rifampicin, isoniazid, and Ethambutol, and one month of RHZE. The second phase is the continuation phase, which comprises five months of Rifampicin, isoniazid, and Ethambutol (RHE).

Note: For TB meningitis and bones, treatment is 12 months.

Multi-Drug Resistant TB: when TB is resistant to first-line drugs, treatment takes a minimum of 20 months.

TB Treatment Principles

- Use the correct drugs and dosages.
- Ensure that all phases of treatment are given under strict supervision.
- Ensure regular clinic attendance for the full duration of the continuation phase.
- Avoid treatment interruption.
- Keep accurate records of patient information and clinic attendances.
- Maintain uninterrupted drug uptake.

Follow-Up for TB Patients

- Implement DOTS with CHVs.
- Involve close relatives to create a suitable home environment for treatment (e.g., psychological and physical support).
- Give health education to close family members and relatives to create positive attitude towards the patient and reduce stigma.
- Provide information, education, and communication (IEC) materials in the form of pamphlets, for patients and relatives to be more informed in order to increase adherence.
- CHVs should remind patients on follow-up sputum examinations at the second, fourth/fifth, and sixth/eighth months of treatment.
- Refer TB patients to the health facility for further treatment in case of any complications.
- Ensure proper updating of patient records.
- Provide counselling to patients on adherence to TB treatment.

Side Effects of TB Drugs

Community health volunteers should immediately report all side effects to the nearest health facility.

Social Support

Nutrition Support

Nutrition is the process of receiving or supplying food to the body to grow, function, and maintain health.

Nutrition Management for TB Patients

- Screen for malnutrition – MUAC.
- Nutrition education/counselling.
- Food and nutrients support.
- Linkage for nutritional support.

Key Messages in Nutrition and TB at community level

- Eat a variety of balanced foods every day.
- Consuming locally available foods saves money and time.
- Eat fruits in season as they are cheaper; concentrate on yellow and red fruits.
- Prepare meals in hygienic conditions.
- Food preservation is important to maintain the quality of food, but avoid using non-nutritional products (e.g., Magadi soda) that destroy nutrients.
- Maintain optimal nutrition status whilst on TB treatment to prevent wasting.
- Drink at least eight glasses of clean water every day.
- Breastfeed infants exclusively for six months to create strong immunity.
- TB drugs are safe in breastfeeding.

Food-Based Interventions at Community Level

- Addressing food insecurity at household level to promote adherence and improve cure rates. This can be done by linking the needy patients to food programmes.
- NON STATE ACTORSs, partners, and others should advocate for the provision of general food rations, available social protection package, giving food vouchers or tokens.

TB Infection, Prevention, and Control at the Community Level

Infection Prevention and Control

Prevention of TB transmission and infection in the household and health facilities is an important component of control and management of TB. Infection prevention and control is an effective method of preventing the transfer of disease-causing microorganisms/germs amongst health care providers, patients, and community. This can take place within the health care settings, community settings, and congregate settings such as military camps, schools, etc.

Methods of TB Infection Prevention and Control

There are many ways that CHVs can educate the community on infection prevention and control of TB. These methods include:

- **Improved ventilation and lighting**

  TB is spread through the air, and hence it is important to have doors and windows open most of the time to allow air to circulate. The rooms should have adequate and natural lighting, as light kills germs that cause disease. In houses that have poor lighting and ventilation, the TB patient should be encouraged to spend as much time outside as possible.

- **Cough etiquette**

  It is important to cover your mouth when coughing, as well as to cough facing away from the people, as this reduces the spread of germs.

- **Proper handling of sputum**

  The patient should be advised to provide the sample sputum outside in the open air. The sputum should be covered with a tight lid and taken to the health facility for testing.

- **Personal protection**

  Community health care workers should protect themselves from infection in high-risk environments by using N95 masks, whilst the TB patients should wear surgical masks. These environments include MDR clinics, etc.

- **Early diagnosis**

  It is important that any person that has a cough visits the health facility and is screened for TB before the infection progresses and makes the person ill.

- **Immediate initiation of treatment of infectious cases**

  It is important that once a person is started on treatment early, they should be given the necessary support in order to complete the treatment.

- **Administering DOTS for confirmed cases**

  A TB patient needs to be observed whilst taking TB medication by either a health worker or family member. This encourages the patient to take and complete the course of medication.

- **Prevention of HIV infection**

  TB patients on treatment should receive education on HIV prevention, as a combination of the two infections will weaken the immune system more and may cause death, whereas TB has a cure.

- **Contact tracing/invitation and health education**

  Contact tracing involves household visits of families of those who have been diagnosed with TB to offer them information, counselling, and advice on how to handle and manage TB. They are encouraged to get tested for TB, as they spend time with the client and TB is spread through the air, and they could be at risk.

- **Isoniazid preventive therapy for children and people living with HIV**

  Smear-positive mothers should spend limited time with their child so as to avoid infection and should observe cough etiquette at all times. The child should also be taken to the health facility for screening for TB and, if found not to have TB disease, they should be put on IPT (Isoniazid Preventive Therapy)

- **Tracing TB treatment interrupters**

  It is important for one to complete his/her treatment, as failure to adhere will result in MDR-TB, which takes a longer time to treat. Clients who interrupt treatment should be traced to their homes and brought back to the health facility for treatment.

- **Vaccination with Bacillus Calmette–Guérin (BCG)**

  All children should receive BCG vaccination at birth or, if the children are born at home, the mother should take the child to the health facility.

- **Good nutrition**

  Eating a balanced diet of carbohydrates, proteins, and vitamins can prevent TB infection. Children who are malnourished should be screened for TB and referred for nutritional counselling. Those people on TB treatment should receive advice on how to eat a balanced diet so as to improve their health.

Social Determinants of Health

The social determinants of health are defined by WHO as the conditions (including health systems) in which people are born, grow, live, work, and age. These circumstances are shaped by the distribution of money, power, and resources at global, national, and local levels which are themselves influenced by policy choices. The social determinants of health are mostly responsible for health inequities, which are the unfair and avoidable differences in health status seen within and between countries. In public health, it incorporates not only social factors influencing health, but also economic, cultural, or environmental factors, including laws and policies as well as those operating from community norms.

There are five determinant areas that reflect a number of critical components/key issues that make up the underlying factors in the arena of social determinants of health.

Economic Stability

- Poverty
- Employment Status
- Access to Employment
- Housing Stability (e.g., homelessness, foreclosure)

Education

- High School Graduation Rates
- School Policies that Support Health Promotion
- School Environments that are Safe and Conducive to Learning
- Enrollment in Higher Education

Social and Community Context

- Family Structure
- Social Cohesion
- Perceptions of Discrimination and Equity
- Civic Participation
- Incarceration/ Institutionalisation

Health and Health Care

- Access to Health Services—including clinical and preventive care
- Access to Primary Care—including community-based and preventive care
- Health Technology

Neighborhood and Build Environment

- Quality of Housing
- Crime and Violence
- Environmental Conditions
- Access to Healthy Foods

Reference

i. Velema JP, Ogbeiwi OI.(2007). Organisations should strive for high BCG coverage in communities at risk of leprosy. Lepr Rev.;78(2):88-101.;

ii. Merle CS, Cunha SS, Rodrigues LC(2010). BCG vaccination and leprosy protection: review of current evidence and status of BCG in leprosy control. Expert Rev Vaccines. 9(2): 209-22.

iii. Zodpey SP, Ambadekar NN, Thakur A (2005). Effectiveness of Bacillus Calmette Guerin (BCG) vaccination in the prevention of leprosy: a population-based case-control study in Yavatmal District, India. Public Health. 119(3):209-1

CHAPTER 10

ADVOCACY AND COMMUNICATION

Introduction

TB is still a major public health problem in Kenya, despite the significant progress so far made. To address this major global and national public Health problem, the Global Stop TB Strategy emphasizes that advocacy and communication (A&C) should be implemented. This can improve case detection, treatment adherence, combating stigma and discrimination through empowering individuals and communities to mobilize political commitment and resources for TB. A&C includes a set of cross-cutting activities that are relevant to all aspects of the Stop TB Strategy. It can support specific objectives for interventions for TB, TB/HIV, MDR-TB, Childhood TB, Lung Health or other program components which addresses the social determinants of health, cultural, financial, and psychological barriers to successful implementation of strategies.

The Ministry of Health through the NTLD-P has developed Advocacy and Communication guidelines based on TB Communication strategy, Global Stop TB partnership strategy and other guidelines on A&C. The purpose of guidelines seeks to build political will to increase and sustain financial and other resources for TB, and holding authorities accountable to ensure that pledges are fulfilled within an acceptable timeframe, increase case finding and enrollment into care, enhance treatment outcomes and advocating for right and responsibilities of the patient as enshrined in the patient charter and Kenya constitution 2010.

The current Advocacy and communication strategies identify the need to create an enabling environment for prevention lung diseases. Advocacy will target those in positions of authority to influence human, financial and material resources to strengthen the fight against TB, Leprosy and other lung diseases. At the same time, community advocacy will take advantage of community-level structures such as community health volunteers to create public demand for TB, leprosy and lung disease services. In this regard, health care providers are crucial channels of advocacy and communication while at the same time being targeted with messages to counter the risks arising from occupational hazards.

The scope of this guideline seeks to:

a) Raise the profile of TB, leprosy and lung diseases through targeted public and private engagements with stakeholders while promoting highly influential TB ambassadors.

b) Increase the visibility of TB messages to raise awareness and debunk myths and misconceptions regarding TB, MDR-TB and XDR-TB. These will be done

c) through health-related events, such as World Malaria Day, World Diabetes Day, Day of the African Child, Day for the Elderly, and Reproductive Health Day

d) Increase resource allocations to address TB, leprosy and lung diseases as well as resources used to increase awareness of these diseases

e) Promote screening for TB and lung diseases to increase diagnosis and access to care and treatment

f) Normalize TB and by so doing reduce stigma associated with TB by promoting TB ambassadors, celebrity spokespersons, testimonials and public discourse on TB

g) Increase disclosure of current and past TB patients to increase treatment adherence and reduce stigma.

Advocacy

Kenya's health sector has recently undergone fundamental changes in structure and funding. The 2010 Kenya Constitution Act changed the system of governance from a centralized to a devolved system with the county as the operational unit for the Ministry of Health. Whereas development of health policy has remained at the national level, service delivery has devolved to the 47 counties. The most important implication of this is that the management of health resources was devolved and placed under the management of the county government under the leadership of the governor and the county health executive. This shift in control of material, financial and human resources from the national level to the county levels means that advocacy efforts to ensure resources for TB, leprosy and lung disease programs must be directed to the county level. This advocacy guidelines therefore identifies the county-level leadership as a key target for both advocacy and communication to (a) raise the profile of TB, leprosy and lung diseases at the county level and (b) raise awareness of the need for prioritization of resource allocation towards control of TB, leprosy and lung disease. Every individual must feel empowered and obligated to stop TB.

At the national level, the program head together with the Stop TB partnership will together work on strategies to lobby parliamentary caucus on TB, treasury, Ministry of health, donor partners to ensure that resources are allocated for TB, Leprosy and Lung Disease activities.

At the national level, the program head together with the key partners work on the strategies to ensure branding of National TB, Leprosy and lung disease program in order to raise the profile of TB, Leprosy, and lung Diseases both at the country and international level.

At the County level County director of health /CEC for health and CHMT will work on the strategies to lobby county government to ensure that TB, Leprosy and Lung Disease activities are reflected in the county integrated development plan and resources allocated in annual work plans and budgets. The activities/event to be lobbied for consideration should include the following but not limited to, world TB day, World Asthma, world Leprosy day, and world Diabetes day

At the community level the community health extension workers together with Community health volunteers and civil society organizations work on the strategies to advocate for communities to demand for TB, Leprosy and Lung Disease treatment and care at the community level

Planning for advocacy sessions

The following forums can be used to conduct advocacy sessions which also include the use of the celebrities and former TB patients, recovered leprosy patients and Asthma patients:-

- Courtesy calls to prominent personalities
- Stakeholders forums
- National days
- World Health days i.e. World TB, Leprosy and Asthma days
- Agriculture society of Kenya shows
- Mass media, social media, celebrities shows like church live shows

Monitoring and Evaluation Framework and key IMPACT TARGETs

Regular monitoring and evaluation of implementation activities will be done at all levels of implementation and will be guided by the National Strategic Plan (NSP). Routine monitoring will track the processes through programmatic reports and feedback from the communities while evaluations will focus on the outcome and the impact of the various interventions. Impact targets are outlined below.

General

1. Increase case notification of new TB cases to 85% of estimated prevalence by 2017. Communication activities will seek to reduce real and perceived stigma associated with TB to increase positive community TB intervention. We intend to see more cases referred for screening and an increase in those enrolled into care. Stigma is mainly caused by myths and misconceptions among the general public and Health Care Providers.
2. Ensure treatment success of at least 90% among all drug-sensitive forms of TB, and among all age groups, by 2017. Communication will be used to promote self-adherence as well as community involvement in adherence support. Communication will emphasize the role of the family as treatment support.
3. Increase case notification of DR-TB to at least 75% of estimated prevalence (baseline TBD: DR survey) Communication activities will seek to reduce real and perceived stigma associated with DR-TB to increase positive community DR-TB intervention
4. We intend to see more cases referred for screening and an increase in those enrolled into care
5. Reduce real and perceived stigma suffered by PLWHIV. Communication will be used to differentiate HIV from TB and clarify the link between the two diseases. Messages will also be crafted to support treatment seeking and adherence.
6. Increase resource allocation from the current as internationally agreed; raise awareness of the need for prioritization of resource allocation towards control of TB, leprosy and lung disease at all levels

Pediatric Lung health

Reduce the average number of annual acute episodes for children with asthma by 15% in areas with established asthma clinics. Communication activities will focus on raising awareness of the risks of TB among children and the risk posed to children in contact with persons with TB. The need for early diagnosis will be emphasized, as will symptoms among children.

Asthma

Increase to 80% the proportion of controlled asthma patients. Communication activities will concentrate on raising awareness of the risks posed by asthma, to allay misconceptions and myths regarding the management of asthma.

Communication

Within the context of a newly devolved health system, the goal of the National Strategic Plan (NSP) is to accelerate the reduction of TB, leprosy and lung disease burden through provision of people-centered, universally accessible, acceptable and affordable high-quality services in Kenya.

To achieve this goal, multi-media and targeted communication approach will be used. It will combine use of mass media, social media and interpersonal media so that all key populations are reached.

Communication Channels

The communication scene in Kenya is dynamic and has changed dramatically over the past years. Mass media have expanded exponentially. Radio stations have been on the rise ever since the liberalization of the media. In 1999 there were fewer than 10 local radio stations in Kenya, but now there are more than 116 radio stations in Kenya with wide coverage and listenership. Television stations have increased from 4 to 15 between 1999 and 2010. There are local stations and large international broadcasters such as BBC, CNN and CCTV. Digital TV is also available such as Zuku, Go-TV, SmartTV and DSTV offering operating as a pay per view stations. The number of daily national newspapers has increased. The two widely read newspapers, the *Daily Nation* and *The Standard*, are now rivaled by *The Star* and *The People*. There are also regional papers such as *The East African* and specialized ones like *Business Daily*. However, the biggest growth since 2006 has been in the area of digital communication. The number of Kenyans accessing the internet has increased dramatically. Kenya now boasts 14.032 million internet users, accounting for 28% of the population and an internet penetration of 75% nationally. The growth of social media in Kenya is phenomenal; the number of Kenyans using Facebook stood at 2,045,900, or 4.8% of the population, while the number of Kenyans using Twitter is second highest in Africa at 2,476,800. The number of Kenyans 'blogging' on a regular basis has also risen. The proliferation of internet-enabled mobile phones has also meant that more than 3 million people now have access to online communication as well as personal radios, thus increasing reach by huge margins from the 2006 figures. Mobile telephony has increased connectivity, with the number of SMS sent annually growing as reflected in the revenue growth. The digital platforms present great opportunities that are yet to be exploited by health communication in general, and for communicating about TB, Leprosy and lung health in particular.

Communication on matters concerning health is still very personalized, and peer-led interventions carry a lot of weight. Communicating health benefits as well as raising awareness of health facilities and services can be effectively and efficiently provided by the mass, print and social media, but the more personal communication needed for behavior change is better handled thorough interpersonal communication. Social media promises high potential to build community-level advocacy and raise awareness on health issues. There is room for exploration of mobile phone-based reminder systems to promote TB screening, treatment adherence and reminders about high-risk behavior such as alcohol consumption. But where there is a need for complete reinvention of cultural norms, such as cough etiquette, the traditional channel of communication will be more effective.

Communication on Adherence to Treatment

The aim of the National TB, leprosy and lung Disease program is to successfully treat at least 90% of all patients started on treatment. This can only be achieved by ensuring good compliance to treatment. This can be done where there is a good communication strategy for patients being started on medication. TB is curable if patients take a complete and uninterrupted course of the appropriate medicines for treatment. However, poor compliance to TB medication is a common problem. Treatment interruption presents a problem for patients, for their family and community and for the health care personnel caring for them.

The consequences of inadequate and incomplete treatment are serious and could lead to the following:

- Prolonged illness and disability for the patient.
- Infectiousness of the patient causing continued TB transmission in the community.
- Development of drug resistant TB.
- The possibility of death.

Due consideration should be given to the many factors that can adversely influence treatment outcomes.

Factors that Influence Treatment Outcome

Table 10.1: Factors that Influence Treatment Outcome

Social and Economic Factors	Health System Factors
Extreme poverty	Poor health infrastructure
Poor support networks	Poorly trained or supervised health care personnel
Unstable living circumstances	Low levels of accountability of health staff
Drug and Substance abuse	Poor relationships with patients
Myths and misconception	Inadequate development of community based support system for patients
Values and belief about TB and its treatment	

Patient related factors	Treatment related factors
Stigma	Complex treatment regimens
Depression	Large pill burden
Disempowerment	Adverse drugs reactions
Poor knowledge about TB and the efficacy of treatment	Long treatment duration

A comprehensive approach needs to be adopted, that addresses all these issues in order to improve treatment compliance. Particular attention should be paid to factors within the health care system, such as access to services and the attitude and behavior of health care providers as these lie within our spheres of influence.

Strategies for good adherence

In order to achieve good adherence to TB treatment the following steps must be followed at the start of TB treatment.

- Adherence to treatment means following the recommended course of treatment by taking all the prescribed medications for the entire length of time necessary.
- Patients' adherence is a key factor in treatment success.
- Promoting adherence through a patient centered approach that includes facilitating access to treatment, choosing with the patient the most convenient time and place for direct observation of treatment and, when possible, providing other social and medical services, is much more effective than spending resources on defaulter tracing
- Convenience to the patient must be balanced with the assurance of regular drug intake and monitoring,
- Important to give the patient the best chances of cure. When patients receive self-administered treatment, they often take drugs irregularly, and tracing is difficult and often unproductive.
- In addition, there is a much longer period between interruption of treatment and initiation of treatment after tracing the patient.
- It is vital for health staff and community workers to offer polite and efficient attention, and to consider the patient's needs at every contact with the patient.

Getting to Know Your Patient

Obtaining Patient Information

For you to provide care that addresses the specific needs of your patients, it is important that you learn as much as possible about your patient's medical and social history, beliefs and attitudes about TB, sources of social support, and potential barriers to treatment adherence, close contacts.

Assessing your patients' perceptions about TB

Understanding your patient's perspective is an important step toward ensuring adherence. However, the most important point to remember about assessing your patients' perceptions about TB is to first create an atmosphere of trust and acceptance so that your patients will feel comfortable discussing their thoughts with you.

Assessing for Adherence

Health care workers often do not know that a patient is not following their recommendations. It is very important for you to determine whether your patients are taking medications as prescribed. Your first responsibility is to be aware of the general problem of non-adherence and to have a high index of suspicion. Consider several methods for assessing adherence.

a) Indirect Methods

Ask the patient whether he or she will be able or willing to take medications for the prescribed time. Ask for specific information:

- How often the patient takes medication
- The number of tablets taken
- How the patient remembers to take the medication
- Whether the patient has problems with the medications

Be sure to listen carefully and assure the patient that the information he or she tells you is very important.

Monitor pills and appointments

Check the patient's response to treatment by asking yourself:

- Has the patient's sputum result improved or converted to negative?
- Does the patient show general improvement?
- Have the TB symptoms improved or disappeared?

Address incorrect medicine taking by asking the following questions:

- Have you had any difficulty taking your pills?
- Over the past week, do you think you have taken your medicine as you should, on time and regularly?
- In general how often do you take the pills?
- In the past week, was there any time you missed taking your pills for more than one day?

b) Direct Methods

Directly observing your patient swallow each dose of medication is an effective method of ensuring adherence

Strategies for improving Adherence

a) In adults

Quality interaction with the patient:

- Create a partnership
- Ask patient whether they do take the TB drugs and do not assume that they do.
- Give each patient adequate time at each visit.
- Be positive do not intimidate or frighten the patient.
- Treat the person and not the disease.
- Understand and address different cultural beliefs and values.
- Adapt treatment to lifestyle.

Make referrals to social welfare, where necessary.

Patient education:

- Give the vital information to the patient on diagnosis
- Be conscious and clear with instructions, as the patient might be anxious after hearing the diagnosis.
- Be clear about the duration of the treatment regimen.
- Do not overload the patient with too much information at the same time.
- Use educational materials that are culturally and linguistically appropriate for the patient.
- Assess the patient's beliefs about TB and if possible integrate the beliefs into the treatment plan.
- Review instructions, question patient to ensure understanding.
- Clarify patient's questions and respond clearly.
- Give written instructions.
- Describe specific adherence behaviors required.

During treatment:

- Modify the treatment plan to patient's suitability, offer options to the patient.
- Give clear instructions about medication side effects.
- Ensure proper record keeping for each patient on treatment.
- Follow up quickly on missed appointments.
- Fast track patients coming for treatment and follow up
- Ensure that staff is supportive to patients
- Ensure that the physical environment is comfortable to patients
- Ensure confidentiality.
- Offer a holistic approach in addressing the patients' needs.

b) In children and adolescents

Children with TB present specific problems for adherence. However there is very little information about the rates of adherence among children or methods for addressing it. To improve adherence among children working with the parents or caregivers who will administer medications to the children is important. You cannot assume that parents will give the medication as prescribed, as some parents are non-adherent.

Provide anticipatory guidance:

- Talk with parents about the potential problems they might experience once treatment is initiated.
- For example, a child may resist taking medication, experience adverse reactions to the medication or have difficulty in swallowing medication.
- When parents are aware of potential problems they may be better equipped to deal with them and assist with the treatment.

Adolescents are at high risk of poor adherence because of concerns about stigma; they may not take their TB seriously; they may feel embarrassed about having to take TB treatment and concerned about what their friends think.

Ensure the following has been obtained:-

a) Patient's residential and work physical addresses and contact details are correct

b) Details of people that the patient has been in contact with in the past three months and stress the need for them to be screened for TB Patient education plans should include information on several topics:

- Patient concerns about the disease, treatment, and follow-up care
- What causes TB?
- How TB is transmitted?
- Diagnostic tests and the meaning of the results
- Infection control measures
- Contact testing and evaluation
- The importance of following a healthy lifestyle
- Use simple, non-medical terms.
- Limit the amount of information you present in any one visit.

Adherence counseling must be structured in such a way that it includes the following aspects:

- Medication that the patient will be taking, when and how to take it, the side effects they may experience from the medication and what to do when the side effects develop.
- The duration of treatment; important milestones during treatment such as sputum testing to monitor the response to treatment and changes in medication; the importance of completing treatment
- Expected benefits of adherence
- Expected consequences of non-adherence
- Developing an adherence plan to identify barriers to treatment and address these to ensure treatment completion

The link to HIV and the need for a HIV test. General health issues including how to eat a balanced diet using readily available food, exercising, stopping smoking and reducing alcohol intake.

It is helpful for clinic staff or a community health worker to accompany the patient to their home. This allows verification of the patient's exact address. It provides an opportunity to arrange for screening of all household contacts, including other symptomatic household members and children under the age of 5 years and those who are HIV positive who require TB prophylaxis. Identify social problems that could impact on adherence to treatment.

Patients' Rights

To ensure the realization of the right of access to health care services as guaranteed and enshrined in Kenya Constitution 2010. The Ministry of Health through National TB, Leprosy and Lung disease program is committed to upholding, promoting and protecting this right and therefore proclaims this PATIENT'S RIGHTS CHARTER as a common standard for achieving the realization of this right:

- A healthy and safe environment
- Participation in decision-making
- Access to healthcare·
- Knowledge of one's health, insurance/medical aid scheme
- Choice of health services
- Be treated by a named health care provider
- Confidentiality and privacy
- Informed consent
- Refusal of treatment
- Be referred for a second opinion
- Continuity of care
- Complain about health services

Responsibilities of the Patient

Every patient or client has the following responsibilities:

- To take care of his or her health
- To care for and protect the environment
- To respect the rights of other patients and health providers
- To utilize the health care system properly and not abuse it
- To know his or her local health services and what they offer
- To provide health care providers with the relevant and accurate information for diagnostic, treatment, rehabilitation or counseling purposes
- To advise the health care providers of his or her wishes with regard to his or her death
- To comply with the prescribed treatment or rehabilitation procedures

- To enquire about the related costs of treatment and/or rehabilitation and to arrange for payment
- To take care of health records in his or her possession

Develop a treatment plan for the patient

A clear treatment plan needs must be developed highlighting the important steps such as dates when sputum must be collected, medication changed and treatment completed. These dates should be clearly documented in the patients' record card, the patients' appointment card and the TB facility register/ appointment diary as a reminder to both patients and staff. Advise the patient to inform clinic staff of any temporary or permanent change of address to facilitate continuation of treatment and of any movements over the treatment period to plan treatment during visits that may take place away from the area. If the patient unexpectedly travels away from the area advise to take the appointment card with them and to present it to the nearest clinic for treatment.

Social, economic, and health problems other than TB may hinder the patient's progress toward completing TB treatment. To minimize the effects of these problems on treatment, develop a problem solving strategy which should be included in this plan.

Directly observed treatment (DOT)

Directly observed treatment means that a treatment supporter watches the patient swallowing the tablets, in a way that is sensitive and supportive to the patient's needs.
Close supervision and monitoring of patients ensures treatment compliance and early detection of adverse side effects due to medication.

The treatment supporter may be a health care worker or a trained workplace or community health worker, family member or whoever the patient chooses. The role of the treatment supporter is to motivate patients to continue treatment and to counter any factors that might result in treatment interruption.

The DOT services must be organized to suit the patient's circumstances and where possible treatment should be provided as close to home as possible. Patients who live close to a clinic may take their treatment at the clinic if convenient for them. There must be a fast tracking system for these patients and good infection control to minimize the risk of re-infection. The following must be conducted at each encounter with the patient:

- Ask about side effects the patient may be experiencing and record in the patient record card
- Provide treatment for minor side effects
- Refer patient to professional nurse or doctor if serious side effects
- Report the side effects to the Pharmacy and poisons board (pharmacovigillance)
- Give the patient their daily dose and observe intake
- Record doses taken in patients' appointment card and patient treatment record.
- Update the facility register/ TB patient diary to identify patients who did not present for DOT on that day and recall them rapidly.

Educate patient about treatment compliance

- Medication for the weekend must be pre-packed for collection on Fridays and responsibility allocated to a family member to observe and indicate on the appointment card for doses taken on weekends.
- Community DOT has the advantage of being more accessible and convenient to patients.
- A TB patient who has far to travel for treatment is less likely to adhere to treatment and community based DOT can be a viable alternative. In some areas, limited resources and high TB caseloads overwhelm clinics; using community-based DOT may contribute to a more rational use of limited resources in these settings.
- The treatment supporter can be a community health care worker or any community/ family member trained to provide DOT.
- Integration of this work within that of the community health volunteers will allow for a sustainable community care program.
- The community treatment supporters must be accountable to the facility manager.

Criteria for assigning treatment supporters

It is impossible to predict who will or will not take their treatment regularly, therefore appropriate support mechanisms should be put in place for the following patients. The following patients must be prioritized for treatment support;

- Children
- Elderly or infirm patients
- Patients with a history of interrupting treatment
- Patients with a history of substance or alcohol abuse
- Patients who are homeless or live under poor social conditions
- Patients with mental illness
- Patients who request a treatment supporter

Members of the patient's family should be encouraged to provide support and motivate the patient to complete treatment. At initiation of treatment, the family member or friend should be counseled together with the patient, so that they have all the information necessary to help the patient complete treatment. One of the difficulties with involving family is that underlying family dynamics can adversely influence treatment. Therefore when selecting a family member or friend to assist with treatment, it should be someone the patient trusts, respects and has a good mutual relationship with.

Engaging NGO/ CBOs in providing community TB care

The following must be considered where there are NGOs/ CBOs providing community care services;

- Mapping of NGO'S providing community care services and determining how they might be able to contribute to community TB care
- Involving community representatives in the selection of community treatment supporters and ensuring an appropriate geographic spread of treatment supporters.

- Establishing a written contract with the community organization and between the community organization and the treatment supporter, defining roles and responsibilities and the standards required.
- The contracts should clarify whether incentives will be made available and under what terms.
- Providing adequate training to CHW on TB:
- Transmission, prevention, screening, diagnosis, treatment, side effects; monitoring response to treatment, HIV care, record-keeping; counseling.
- Working with the community organization to provide regular supervision, support, feedback and motivation of treatment supporters to ensure that quality outcomes are maintained.

Addressing ethics and confidentiality

Establishing standard operating procedures and systems for:

- Administering daily medication.
- Monitoring adherence, including completion of the patients' appointment card when doses are taken and methods for identifying those interrupting treatment.
- Follow-up and recall of treatment interrupters.
- Communication and feedback to clinic.
- Reminding patients about sputum tests that are due during the course of treatment.
- Record keeping at the clinic indicating the location of treatment supporters and patients allocated to them.
- Providing regular feedback to the organization on TB program results and audits; addressing problems through joint problem-solving; acknowledging the community contribution to TB care.

The TB support team

In sharing responsibility for treatment outcomes, the roles and responsibilities of the TB support team need to be clarified. Building a good relationship between members of the team and the patient can help improve adherence. This can be achieved through:

- Creating a sense of partnership between the TB support team, the patient and their family
- Emphasizing the importance of the patient (and family) taking responsibility for treatment, supported by health care personnel
- Giving the patient adequate time at each visit
- Treating patients with respect and consideration
- Being positive; not intimidating or frightening the patient
- Addressing any anxieties the patient may have
- Understanding the patient's cultural beliefs and values.

Roles and Responsibilities of the TB patient

1. Take their tablets as prescribed
2. Report side-effects to the treatment supporter or clinic nurse

3. Return to the clinic for scheduled visits
4. Bring sputum specimens to the clinic for testing at the required times
5. Provide feedback to the team of any problems that they experience
6. Inform treatment supporter and clinic staff if they are going away and make plans for taking medication whilst away
7. Take responsibility for completing their treatment

Roles and Responsibilities of the TB treatment Support Team

- Provide emotional support to the patient
- Encourage/remind patient to take their tablets daily
- Supervise treatment on the weekends, or daily if required, and record doses in the patients' appointment card.
- Remind patient to bring sputum specimens to the clinic for testing at the required times
- Motivate patient to complete the full course of treatment
- Report problems to the clinic
- Provide basic information on TB
- Initiate TB treatment and explain how to take the tablets
- In consultation with patient, allocate to DOT that is most suitable for them
- Provide daily treatment at the clinic for patients receiving Clinic DOT.
- Keep a record of where all patients registered at the facility are receiving DOT
- Complete clinical records: clearly indicate when sputum tests are due; update records (record cards)
- Update the TB facility register
- Assess patients on a scheduled basis, monitor response to treatment, encourage treatment completion
- Provide weekly/two weekly treatment to the patient receiving DOT in the community or workplace
- Get feedback from treatment supporters on patients receiving community DOT
- Arrange transfer of patients moving to another area
- Arrange tracing of patients who have defaulted treatment

Treatment Supporter

- If possible, visit patients commencing treatment at their homes: assess and refer other suspects and contacts to the clinic; identify problems in the household that might affect adherence and report these to the clinic; confirm the patients address
- Meet with patients on a daily basis (including over weekends if possible) and supervise their treatment
- Complete the patients' appointment card to record doses taken
- Ensure that patients have collected their weekly/two weekly medication

- Provide support to TB patients and their families
- Motivate TB patients to complete their treatment
- Remind TB patients to bring their sputum to the clinic for testing at the appropriate times
- Provide regular feedback to the clinic on their patients
- Trace patients who have interrupted treatment
- Create awareness in the community about TB and HIV

Adherence counselor

- Provide structured education and counseling to patient
- Prepare patient for completing their TB treatment
- Assist the TB patient in anticipating problems with adherence and planning ways to overcome these
- Offer additional counseling to patients having problems with adherence

CHAPTER
11

MONITORING AND EVALUATION

Scope of the guidelines

This chapter highlights monitoring and evaluation system for the program which includes: tools used in recording and reporting in TB control in Kenya, processes and mechanisms in place to ensure quality of data, timely reporting and utilization of gathered information to improve the program.

Target Audience

The guideline targets Health Care Workers(HCW) working in health facilities to provide them with reference document when using tools in TB control, county health managers and implementing partners charged with mentorship and capacity building of HCW.

Introduction

Monitoring is the systematic collection, analysis and use of information from projects and programs for purposes of learning, accounting for resources and decision making. Evaluation on the other hand is a time specific assessment of results that can be attributed to program activities. It uses routine monitoring data and, often, indicators that are not collected through routine information systems. A well designed evaluation should allow for the causes of failure to achieve intended results to be identified.

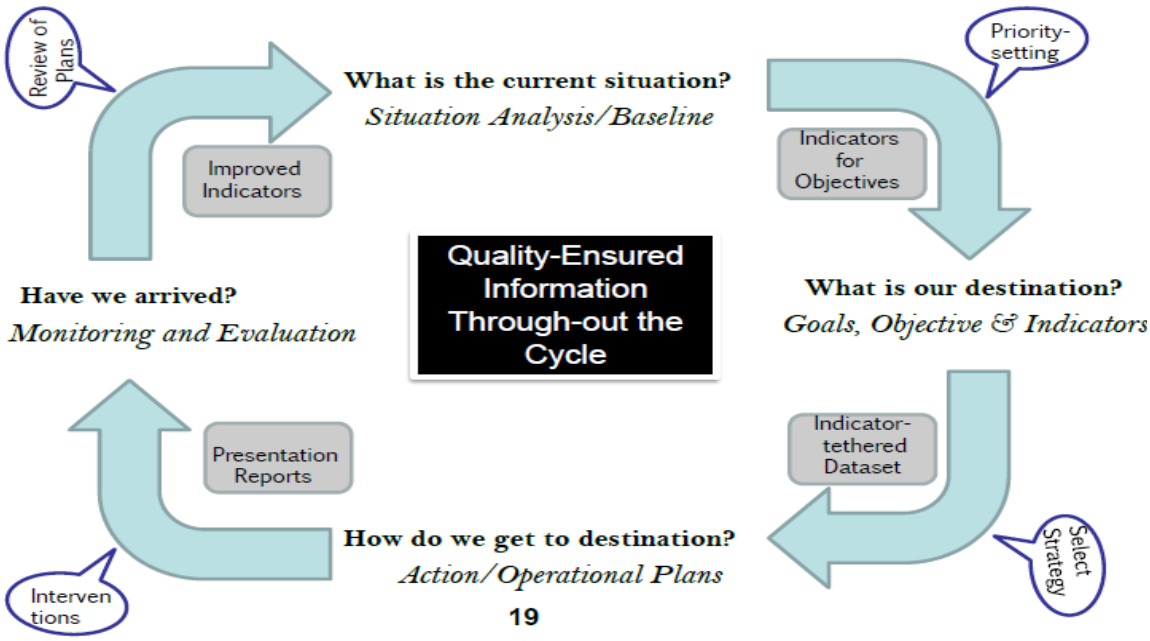
It is inevitable for the program to adopt a robust Monitoring &Evaluation (M&E) function to guide in performance management. Given that the program function involves implementation of various global and local interventions, a well-functioning M&E system helps in measuring whether results are being achieved and how or why they are or not being achieved. M&E forms the basis for clear and accurate reporting on the results achieved by an intervention. A good M&E system is required at every level in the health system, characterized by the following:

- Clear goals, objectives and targets (that are cumulative, with facility targets leading to sub- county targets leading to county targets that build up to national targets)
- Selection of indicators which are valid, reliable, specific, operationally feasible and comparable over time and in different levels of health care delivery.

- Quality assurance procedures to ensure that quality data is collected
- Timely submissions and processing of data
- Ability to process and analyze data
- Data dissemination in both directions
- Both monitoring and evaluation are done on a "cohort" basis. This ensures that all patients recorded in the register within a specified calendar quarter are accounted for within the analysis.

Monitoring and Evaluation is an important component of in project management cycle as depicted in the figure below;

Figure 11.1: Project Management Cycle



Case recording and reporting of TB, leprosy and other lung disease is an important process for monitoring and evaluating disease control activities at the health facility, county and national levels. Accurate, complete and timely data collection is an overarching guiding principle for the program. Every health care provider who treats TB, leprosy and other lung disease has a professional responsibility to record and report all cases treated using standardized tools provided by the program.

Maintenance of accessible, reliable medical records of all individual cases is a minimum requirement that need to be met by all health care workers involved in the diagnosis and treatment of TB, leprosy and other lung diseases. It is the responsibility of the facility In-charge (I/C) with training and technical support (supervision) from the SCTLC to ensure that recording of details about patients is done properly and correctly. The national TB program is responsible for providing standardized recording and reporting tools which should be used at all service delivery points. Any new tool introduced in the facilities should be approved by National M&E Technical Working Group (TWG).

All patients diagnosed in health care facilities **must** be registered at the start of treatment and confidentiality and safety of the patient information maintained at all levels of patient management. HCW should also develop mechanism to control unauthorized changes in medical records.

Standard recording and reporting tools used in the National TB, Leprosy and Lung Disease Program

The following tools are used in the various aspects of management of TB, leprosy and lung disease:

Tools and SOPs/Job Aids for use in Diagnosis and Management of TB, Leprosy and Lung Diseases

Table 11.1: Tools and SOPs/Job Aids for use in Diagnosis and Management of TB, Leprosy and Lung Diseases

No	Name of Tool	Purpose	Location	Filled By
1	**Patient Record Card**	The card is filled by health worker and acts as patient clinical record card used for clinical notes during treatment	TB Clinic	Clinicians
2	**Patient Appointment Card (TB,IPT, DRTB, Leprosy and Asthma)**	The card is used for scheduling treatment appointments and acts as a treatment reminder to the patient.	Patient	Clinicians
3	**Facility TB Treatment Register (TB 4)**	It is a TB Case listing which summarizes key variables for tracking TB patient progress and outcomes	TB Clinic	Clinicians
4	**Sputum/GeneXpert request form**	Used by clinicians to request for sputum /GeneXpert tests	TB Clinic	Clinicians to request and lab personnel to fill results
5	**AFB/GeneXpert Register**	It is a case listing for all pulmonary TB patients sent for AFB microscopy tests done in the lab.	Lab	Lab personnel
6	**Patient referral form from TB clinic.**	Used for referring patients for management of other conditions than TB	TB clinic.	Clinicians.
7	**Patient referral form to TB clinic**	Used for referring presumptive TB cases from other service delivery points e.g HIV clinic , medical clinics among others to TB clinic	Other service delivery points outside TB clinic	Clinicians
8	**Intensive Case Finding /IPT Card – Adults**	This form is used both for screening of adult HIV patients for TB and recording IPT information for eligible patients	TB and HIV clinics.	Clinicians

No	Name of Tool	Purpose	Location	Filled By
9	**Intensive Case Finding /IPT Card – Peds**	This form is used both for screening of children for TB and recording IPT information for eligible children	TB and HIV clinic	Clinicians
10	**IPT Register**	It is a Case listing which summarizes key variables for tracking IPT patient progress and outcomes	TB and HIV clinic	Clinicians
12	**Culture/DST Log Book** **DR TB Presumptive Register (currently called DR TB suspect register)**	To capture patients whose samples have been sent for culture and DST and results	TB clinic	Clinicians
13	**Culture request form**	Used to request for culture/DST for DR TB surveillance	TB Clinic	Clinicians
14	**DR TB Patient Log Book**	Individual patient management booklet that records all information regarding the patient.	TB clinic	Clinicians
15	**DR TB Register**	DRTB Case listing which summarizes key variables for tracking patient progress and outcomes	TB clinic	Clinicians
16	**DR TB baseline and follow up test request form**	Baseline and follow-up request form for DR TB patient.	TB clinic	Clinicians
17	**Facility Daily Activity Drug Register**	To monitor the use of the TB andDR-TB drugs on a daily basis	TB clinic/ Pharmacy	Clinician/ Pharmacist
18	**FCDRR**	It's a reporting tool for consumption of TB, and DR TB drugs	TB clinic/ Pharmacy	Pharmacist/ clinician
19	**Bin Card**	This card is used to monitor stock of commodities in facility store or pharmacy	Pharmacy/ Store	Pharmacist
20	**S11**	This form is in triplicate and is used to issue out commodities to various service delivery points within the facility	Pharmacy/ Store	Pharmacist
21	**Pharmacovigillance Reporting Tools**	To record and report all Adverse Drug Reactions experienced by patients on anti TB drugs	TB Clinic	Clinicians
22	**Community Monthly Reporting Tool**	Reporting tool for community TB control activities	Facility	CHV
23	**Community Treatment Interrupters tracing form**	Used to track patient who have defaulted TB treatment.	Facility	CHV

No	Name of Tool	Purpose	Location	Filled By
24	**Community TB Screening Form**	It is an ICF cards Used for screening TB in the community	Community	CHV.
25	**Community Referral Form**	Used to refer presumptive TB cases, contact tracing and treatment interrupters from community to the facility for diagnosis and treatment	community	CHV.
27	**Leprosy record card**	The card is filled by health worker and acts as patient clinical record card	TB Clinic	Clinician
28	**Leprosy register**	It is a leprosy case listing which summarizes key variables for tracking TB patient progress and outcomes	TB Clinic	Clinician
29	**Asthma Register**	It is Asthma Case listing register which summarizes key variables for tracking Asthma patient progress.	Outpatient/ Chest Clinic	Clinician
30	**Asthma Record Card**	The card is filled by health worker and acts as patient clinical record card used for clinical notes during treatment	Outpatient/ Chest clinic	Clinician
31	**Presumptive TB Register**	Used to record all presumptive TB cases identified in a health facility for the purpose of intensifying case finding	TB Clinic, CCC, outpatient and inpatient departments	Clinician/Nurses
32	**Monthly Data Chart**	It's a monthly summary chart that shows facility performance in various indicators	TB Clinic	Clinician
33	**Data/Information flow chart**	This is a chart that provides clinicians with information on how information flows from facility	TB Clinic	

Attached to these guidelines are samples of the tools and detailed instructions on how to fill the various sections of each tool.

Electronic surveillance system (TIBU)

TIBU is the national electronic surveillance system for TB, MDR TB, IPT, Leprosy and Lung diseases. The system is a replacement of the former district register used by SCTLCs now referred to as sub county TB coordinator (SCTLC) to register and notify cases to the national TB program. The main reasons for digitizing the register and reporting are as a result of:

- Recommendations for revised forms to increased analyses and reporting requirements
- Under-utilization of existing data to improve TB control and epidemiological research
- Requirement for closer integration with other diseases such as HIV/AIDS and integrated epidemiological analyses

Requirements to improve efficiency and control through better utilization of modern information and communication technology. The advantages of electronic recording and reporting are:

- Improves the accuracy of reporting as it brings compilation closer to the source of the data and removes a level of transcription.
- Improves patient and treatment management through better record keeping and reporting at the facility
- Supports electronic data interchange for patient transferring in or out of facilities
- Computers generally useful for other tasks and improve skills development at facilities.

TIBU collates case based data from the sub county creating a combined data base both at county and national levels. Data entered into the system is from a series of documents, the patient record card being the primary source which later summarizes in the facility register and finally being entered into the electronic system. Records existing in the system are updated on a regular basis every time the SCTLC visits the facility for technical assistance and supportive supervision. Once the data is entered into the system, the SCTLC synchronizes the records with the national database for data to be available both at the county and national level. TIBU is the only system currently being used for case notification and is also linked to DHIS to ensure various stakeholders including Ministry of Health headquarters, donors and implementing partners have access to key indicators needed for decision making. The SCTLC should ensure the data is secure at all times and should ensure all cases are notified within three months of starting treatment.

The national TB program provides the SCTLC's with the necessary infrastructure and support to enable them use the electronic surveillance system effectively. This support includes provision of tablets, monthly data bundles and regular capacity building on system upgrade. Equipment safety is the responsibility of the county and sub county staff and damage or loss of the equipment is not the responsibility of the National Program. . Access rights to the electronic system (TIBU) are provided by the national TB program but only SCTLC's, CTLC's and national program staff have access to patient level data.

Standard Reports

National Tuberculosis, Leprosy and Lung Disease Program has standard reports which are in line with WHO reporting requirements for notifiable diseases which require continuous monitoring and periodic evaluations. The following standard reports should be generated and forwarded to relevant office on the stipulated time:

Table 11.2: Standard report generation

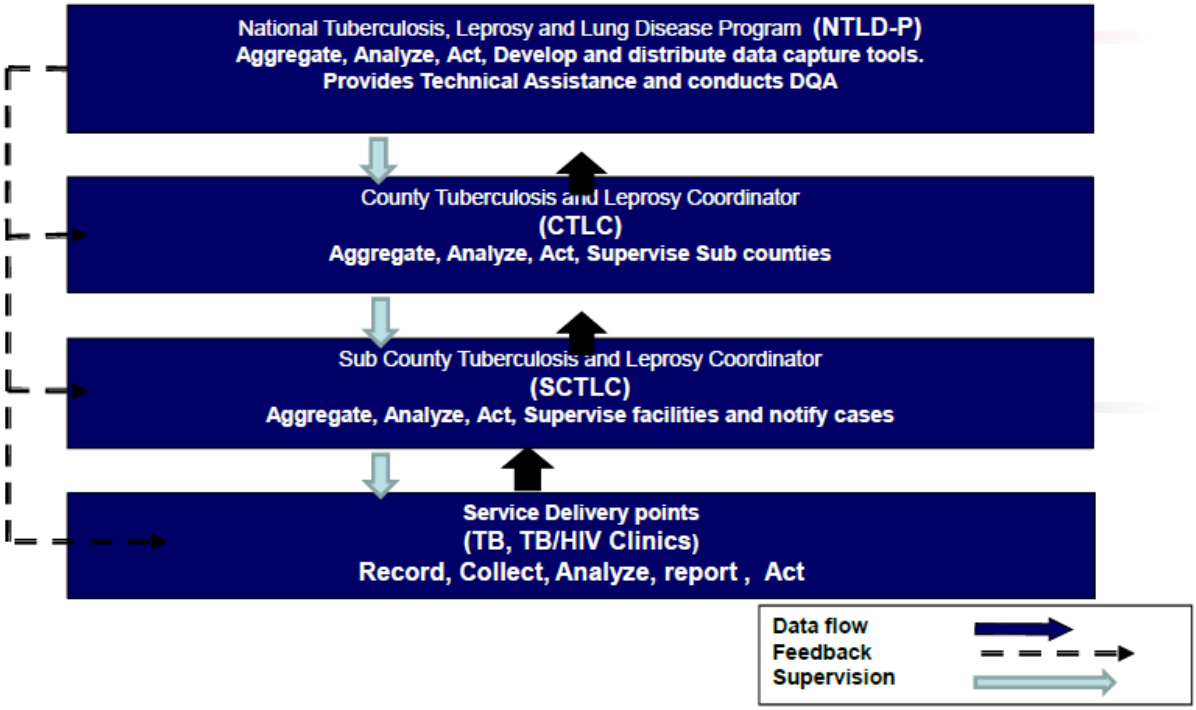
	Name of report	Format	Frequency
1	Case Finding Report (TB,MDR-TB, Leprosy IPT and Asthma)	Electronic (generated from TIBU)	Quarterly
2	Cohort Report(TB,MDR-TB, Leprosy IPT and Asthma)	Electronic (generated from TIBU)	Quarterly
3	Commodity consumption report		Quarterly
4	Pharmacovigillance report		Quarterly

Data Flow and Processing

Data is collected at facility level in the patient record card and later transcribed to the facility register. This should be done routinely. Good data is dependent on the quality of information in the paper- based TB registers.

Timely reporting is fundamental to effective programme management. Reporting is done on quarterly basis and does not mean that data is collated on a quarterly basis; monthly data collation is required at the Sub County level. This will ensure that meaningful action is taken resulting to better patient care and management; effective, efficient and economic use of resources which better inform planning at all levels. The flow chart below shows the various processes that take place at the different levels of TB control in the country.

Figure 11.2: Processes that take place at different levels of TB control in the country



Recommended timelines for recording and data collation

Patient Record cards

The Health Care Worker at the facility will ensure that the patient record cards are duly filled at the start of treatment and subsequent visits as stipulated in the treatment guidelines.

Facility registers

The Health Care Worker at the facility transfers patient details from the patient record card to the facility register at the start of treatment and subsequent visits as stipulated in the treatment guidelines.

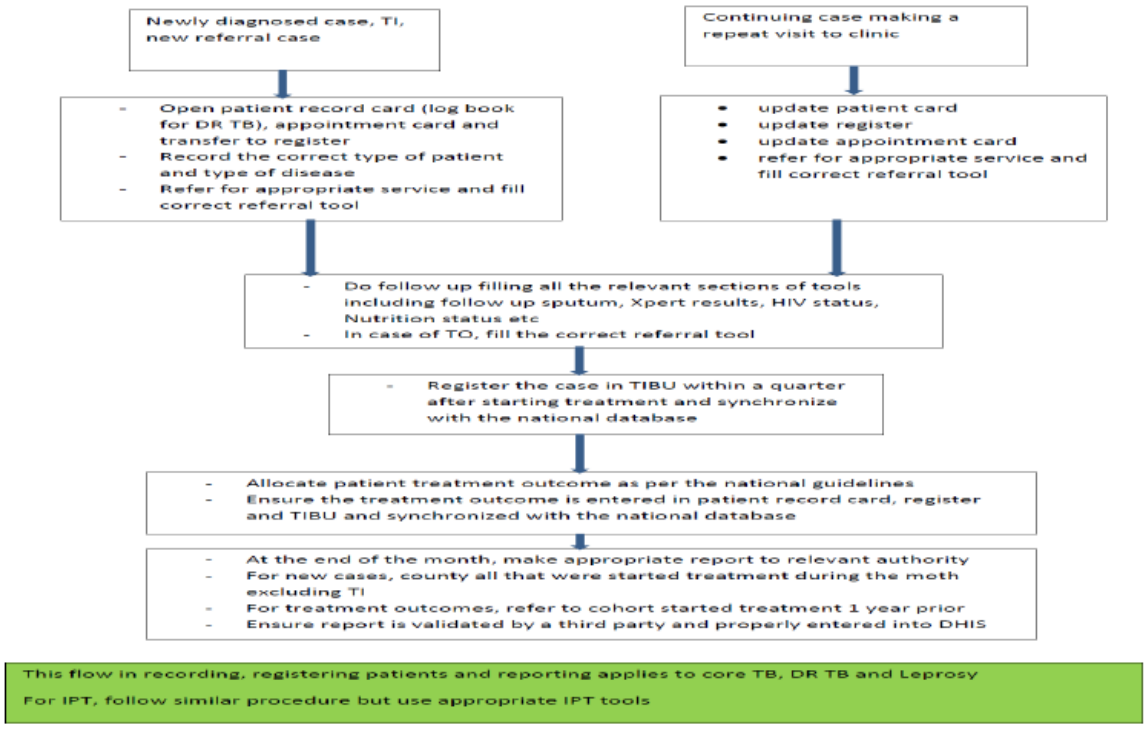
Patient appointment cards

The Health Care Worker at the facility fills the details in the patient appointment card at every clinic visit and allow the patient to carry with them the card as a reminder of next appointment or for presentation to another health facility if the patient is on transit or has transferred.

Sub-County Electronic Register (TIBU)

The Sub County TB and Leprosy Coordinator (SCTLC) shall on monthly basis transcribe patient information from the facility register to the electronic Sub-County Register (TIBU) during regular supervision visits to the facility. They will be required to synchronize the data to the national server from where the county and national registers can be retrieved through patient management system.

The above can be summarized in the figure below:



Data Confidentiality

Security and confidentiality of all routine TB surveillance data should be assured with maximum confidence as desired by the Ministry of Health and the NTLD-P and follow the national laws. All health care workers handling and processing data (both on paper and electronic) should respect the confidentiality of the information collected during all processes taking place in recording and reporting the routine TB surveillance data at all times.

Individuals accessing electronic databases should work only under their own usernames/ passwords and should not share these with others. Individuals should not log on to the system in order to provide another person access to the system. Passwords should be changed if needed and on a regular basis.

Analyzed and published reports should never contain names of individuals or any other identifying information. Access to any data (paper based records or registers and electronic data files both working copies and backups) that allow an individual to be identified should be strictly controlled. Protective measures such as securing data storage media using encryption or passwords should be considered, especially if electronic media are at risk of theft. Data security during transmission needs to take place to safeguard data from un-authorized access.

Data Quality Assurance Mechanisms

Quality assurance is a systematic process of checking whether specified requirements are being met by a specific service or product. Data quality assurance is an important aspect of ensuring sound decision making. The fundamental aspects of data quality including:

- Completeness-All variables in the tools should be completely and correctly filled.
- Timeliness- All cases started on treatment should be recorded and notified within three months of treatment initiation.
- Accuracy – Data collected has enough precision e.g. no BMI without weight or height, weight for age makes sense etc
- Consistency – There is agreement between various tools used to capture data.
- Integrity- There is no unauthorized manipulation of data to meet targets or cover up for poor performance
- Validity – Recording and reporting tools are aligned to performance indicators.

NTLD program has established various mechanisms to safeguard data quality at all levels. These mechanisms include:

- **Annual national data quality assessment:** This a dedicated mission to county and health facilities conducted annually to collect information aimed at ascertaining the quality of data at these levels. The mission is organized by the NTLD program and a standard tool for data quality assessment is used. Counties and facilities to be visited for the mission are randomly selected and at the end of the mission, a report is written and feedback to counties organized through various forums. Immediate feedback to health facilities participating in the mission should be provided and action points with responsible personnel agreed upon during the visit. During such missions, all visited facilities will be expected to produce all documents as requested by the mission delegation.

It is recommend that routine data quality assessment should be carried out by all levels of reporting, national, county, sub county and within the facility.

- **Quarterly data review meetings**: As a means of ensuring data ownership and transparency NTLD-P has organized the 47 counties into 18 clusters to facilitate efficiency in quarterly data review meetings. At a minimum, the meetings should be composed of NTLD-P staff, county and sub county TB and leprosy coordinators, county and sub county medical lab technologists, county pharmacists, other county health management representatives and representatives of implementing partners. The purpose of the meetings is to review all elements of data quality, share best practices, upcoming events and new updates.
- **Technical support to counties and health facilities:** Where data quality gaps are identified through analysis, the NTLD-P may decide to conduct special technical

support to the County/health facility of concern to address the specific gaps using tools that will be developed based on the need. The National Program will provide technical assistance to counties at least once every quarter. The county TB team will carry out teachnical assistance o sub counties and facilities under them at least once every quarter while the sub county TB coordinator will ensure that there is at least one visit to each facility at least once every three months.

Apart from these mechanisms that have been put in place by the national TB program to ensure data quality, HCW in a facility should also be proactive in checking their own data for quality. They should be aware of some of the most common errors observed including

- Missing data
- Duplicate data
- Data capture in wrong box
- Unlikely values for a variable
- Contradictions between variables
- Calculation errors
- Typing error

HCW should employ the following strategies to identify and address these errors:

- Look
  - Across each line
  - Top to bottom
- Look for
  - Missing data values
  - Obvious fluctuations
  - Inconsistencies between data elements
  - Mathematical errors
- Review documentation
- Trace and verify numbers
- Perform "cross-checks" of the verified totals with other data sources
- Perform "spot-checks" to verify the actual delivery of services
- Look for seasonal variations over time, variations outside of the set ranges, and facility comparisons

Data demand and utilization

Facilities providing TB, leprosy and IPT services are expected to utilize the data generated to make decisions and improve management of patients. Facilities through the support of SCTLC should on a monthly basis analyze data and post the results for various indicators to a standard wall chart provided by the NTLD-P or a customized tool meeting the specific needs of the facility. The key indicators that facilities will track at this level will include but not limited to;

1. Number of new TB cases registered disaggregated by type of TB, gender and age.
2. Treatment outcomes: Calculate facility treatment success rate, cure rate etc
3. HIV testing rate

4. ART uptake rate
5. HCW contribution in referral of patients for treatment
6. MDR surveillance
7. Proportion of eligible patients with 2nd month sputum follow up testing

Operations Research

Operations research is research carried out to optimize the use of current TB control strategies and tools at all levels and to operationalize the introduction of new ones by linking their use with epidemiological, operational, behavioral, social, health systems, health economics and policy research. The purpose of OR

- To identify problems during the implementation of Stop TB strategy
- Determine workable solutions
- Test solutions in the field
- Plan for scale up

Facility HCW are encouraged to utilize the routine data for operations research. When using these data for OR purpose, HCW will be expected to follow the following procedures:

- Ensure they have an approved protocol/concept paper from the necessary authority
- Ensure all ethical considerations are adhered to when collecting/abstracting patient level data
- Seek support from SCTLC/CTLC on data analysis and interpretation, report writing
- Follow the laid down procedures in dissemination of results

Any persons seeking to access patient data at the facility for the purpose of research must have an approved research protocol by an ethical review board and authority to access records from county health management

Program monitoring indicators

The following performance and impact indicators shall be tracked by the NTLD program at various levels.

Table 11.3: Performance and Impact Indicators tracked by the NTLD program at various levels

Indicator	Definition	Source of data	Frequency	Level
Treatment Success Rate (bacteriologically confirmed.)	**Numerator:** number of bacteriologically confirmed cured and treatment completed among those started on treatment. **Denominator:** Total number of bacteriologically confirmed cases notified.	Facility TB treatment register and Patient records cards TIBU Cohort report.	Quarterly.	Facility, Sub-county, County and National.

Indicator	Definition	Source of data	Frequency	Level
Treatment Success Rate (all forms)	**Numerator** Number of TB cases (all forms) who successfully completed treatment **Denominator**. Total number of TB cases (all forms) who were notified.	Facility TB treatment register and Patient records cards TIBU Cohort report	Quarterly.	Facility Sub,county County and National.
Number of TB cases (all forms) notified to the national program	Number of TB cases (all forms) notified to the national program	Facility TB Treatment Registers TIBU	Quarterly	Facility Sub county County and National
Number of Bacteriologically confirmed TB cases	Number of Bacteriologically confirmed TB cases that were notified.	Facility TB Treatment Registers TIBU	Quarterly	Facility Sub county County National
TB/HIV				
Number and Percentage of TB patient tested for HIV with known results	**Numerator:** Number of TB patient tested for HIV with known results **Denominator:** Total Number of TB patients all forms notified.	Facility TB Treatment Registers TIBU	Quarterly	Facility Sub county County National
TB/HIV Co-infection rate	**Numerator**: Number of TB patient with HIV positive results. **Denominato**r: Total number of TB all forms tested for HIV**.**	Facility TB Treatment Registers TIBU	Quarterly	Facility Sub county County And National
Percentage of TB patient who tested HIV positive and initiated on ART.	**Numerator:** Number of TB patient who tested HIV positive and have been put on ART **Denominator:** Number of TB patient who tested HIV positive.	Facility TB Treatment Registers TIBU	Quarterly	Facility Sub county County National
Proportion of children under 5 who are contacts of TB patients put on IPT	**Numerator:** Number of children under 5 exposed to smear positive TB patients put on IPT **Denominators:** Number of children under 5 exposed to smear positive TB patients	Contact and IPT registers TIBU	Quarterly	Facility Sub county County National

Indicator	Definition	Source of data	Frequency	Level
DR TB				
Number of laboratory confirmed DR-TB patients enrolled in second line anti-TB treatment	Number of DR TB cases notified	DR TB registers TIBU	Quarterly	Facility Sub county County National
Percentage of eligible TB patients receiving Drug Susceptibility Testing (Molecular and conventional) for DR TB among the people eligible for Drug Susceptibility Testing according to national policy.	**Numerator**: Number of cases done DST. **Denominator**: Number of Cases eligible for DST.	Facility TB Treatment Registers Lab Records ,Gx LMIS. LIMS	Quarterly	Facility Sub county County National
Treatment Success Rate (TSR) among DR-TB cases	**Numerator**: Number of DR TB cases who got cured or completed treatment. **Denominator**: Number of DR TB cases enrolled on treatment.	DR TB registers TIBU	Quarterly	Facility Sub county County National
Nutrition				
Percentage of patients on treatment with BMI recorded in the treatment register	**Numerator**: Number of patients on treatment with recorded BMI in the treatment register. **Denominator**: Number of patients (all forms) on treatment.	TIBU TB registers	Quarterly	Facility Sub county County National
Percentage of patients with BMI under 18.5 on nutrition support	**Numerator:** Number of patients with BMI under 18.5 on nutrition support. **Denominator:** Total Number of patients with BMI under 18.5.	TIBU TB registers	Quarterly	Facility Sub county County National
Leprosy				
Number of leprosy cases notified (by grade)	Number of leprosy cases notified (by grade).	Leprosy register	Quarterly	Facility Sub county County National
Number of health workers trained on Leprosy control.	Number of health workers trained on Leprosy control.	Training Database at the National Level.	Quarterly	Facility Sub county County National

Indicator	Definition	Source of data	Frequency	Level
Number of Skin Screening Clinics held	Number of Skin Screening Clinics held	STLC Quarterly report	Quarterly	Facility Sub county County National
PAL				
Number of patients screened for Asthma	This indicator provides an absolute number of patients screened for Asthma in a particular month	Asthma register/OPD Register	Monthly	Facility
Number of health care workers trained on PAL	Number of health care workers trained on PAL	Training Database	Quarterly	Facility Sub county County National
Laboratory				
Proportion of laboratories performing quarterly External Quality Assurance (EQA) for smear microscopy	**Numerator**: Number of laboratories performing quarterlyExternal Quality Assurance (EQA) for smear microscopy. **Denominator**: Total Number of laboratories performing smear microscopy.	EQA Reports	Quarterly	Sub county County National
Percentage of laboratories showing adequate performance (concordance of 95% and above) among those that received EQA for smear microscopy during the reporting period	**Numerator:** Number of laboratories showing adequate performance (concordance of 95% and above). **Denominator:** Number of laboratories performing quarterly External Quality Assurance (EQA) for smear microscopy.	EQA Reports	Quarterly	Sub county County National
GeneXpert				
GeneXpert utilization rate	**Numerator:** Number of GeneXpert tests done in the period under review **Denominator:** Number of expected GeneXpert tests in the review period.	GeneXpert Register and GX Alert System.	Quarterly	Facilities with GeneXpert machines. County National

Indicator	Definition	Source of data	Frequency	Level
GeneXpert Error Rate				
IPC				
Number of health workers trained as TOT on TB Infection Prevention Control(IPC)	Number of health workers trained as TOT on TB Infection Prevention Control(IPC)	Training Database at the National Level	Quarterly	Facility Sub county County National
Number of TB IPC team members trained on IPC	Number of TB IPC team members trained on IPC	Training Database at the National Level	Quarterly	Facility Sub county County National
Number of Health Care Workers (HCWs) sensitized on facility based TB IPC plans.	Number of Health Care Workers (HCWs) sensitized on facility based TB IPC plans.	Facility Based Reports	Bi-Annually during TA	Facility Sub county County National
Community				
Number and Percentage of patients referred by CHVs	**Numerato**r: Number of patients(all forms) referred by CHVs **Denominato**r: Number of patients (all forms) put on treatment.	TB Register TIBU	Quarterly	Facility Sub county County National
Number and percentage of Patients on DOTs by CHV	**Numerato**r: Number of patients(all forms) on DOTS by CHVs **Denominato**r: Number of patients (all forms) put on treatment.	TB Register TIBU	Quarterly	Facility Sub county County National

Guideline on how to calculate key program performance and outcomes

HCW monitoring the performance at their facility or at sub county and county levels need to use these metrics in calculating some of the key performance indicators.

Table 11.4: Guideline on how to calculate key program performance and outcomes

No	Performance Measure	Definition	Disaggregation	Comment
Treatment Outcomes				
1	Number evaluated	These are all patients with a treatment outcome allocated at the end of their treatment. These number forms the denominator for all treatment outcome measures	Can be disaggregated by smear results (positive, negative and not done)	Refer to treatment section of these guidelines to know when to evaluate
2	Cure rate	Numerator: All cured patients Denominator: All evaluated smear positive patients	Age, gender, sector	Refer to treatment section of these guidelines to know when to evaluate patient as cured
3	Treatment success rate	Numerator: All patients evaluated and have either cured or TC outcome Denominator: All evaluated patients	Age, gender, sector, smear results	
4	Dead (%)	Numerator: All patients evaluated and have dead outcome Denominator: All evaluated patients	Age, gender, sector, smear results	
5	Lost to follow up (%)	Numerator: All patients evaluated and have either cured or TC outcome Denominator: All evaluated patients	Age, gender, sector, smear results	
6	Transfer out (%)	Numerator: All patients evaluated and have TO outcome Denominator: All evaluated patients	Age, gender, sector, smear results	
7	Treatment Failed (%)	Numerator: All patients evaluated and have outcome 'Treatment failed' Denominator: All evaluated patients	Age, gender, sector, smear results	

No	Performance Measure	Definition	Disaggregation	Comment
Service Delivery				
8	% of patients tested for HIV			
9	TB/HIV co-infection rate			
10	% TB/HIV co-infected patients on ARV			
11	Number of TB cases identified and put on treatment			
Laboratory Workload				
12	New presumptive (total)			
13	New presumptive (positive) and %			
16	Total smears done in the month	Total numbers of smear done per month.		
17	Total positive smears and proportion	Numerator. Positive smears Denominator: Total smear done		
TB Burden				
18	Case notification rate per 100,000 population	Numerator: Number of new TB cases (all forms notified. Denominator: Mid year population estimates.		M&E PLAN.

CHAPTER 11

SOCIAL PROTECTION, POVERTY ALLEVIATION AND ACTIONS ON OTHER DETERMINANTS OF TUBERCULOSIS

Background

The new "End TB Strategy" was adopted in May 2014 by the World Health Assembly and sets the required interventions to end the global TB epidemic by 2035. This strategy places a greater emphasis on preventing TB through addressing social determinants of TB, including poverty alleviation policies and social protection programs. The ILO describes social protection as "nationally defined sets of basic social security guarantees which secure protection aimed at preventing or alleviating poverty, vulnerability and social exclusion".

This definition covers protection against:

1. General poverty and social exclusion,
2. Lack of affordable access to health care,
3. Lack of labor market protections,
4. As well as a lack of work-related income.

Examples of social protection programs are but not limited to;

- Noncontributory transfer programs targeted to the poor; cash transfers, food stamps, in-kind transfers, school feeding programs etc
- Schemes that deliver benefits based on contributions of their own members; pensions, unemployment insurance.
- Regulatory aspects of labor; active labor market policies, income support for the unemployed

The global strategy and targets for tuberculosis prevention, care and control after 2015, were endorsed by all member states at the 2014 world health assembly

Reasons for the inclusion of social protection

- Global Challenges
- Global Gaps
- Operational efficiency

To ensure full impact, these actions must build on principles of government stewardship, engagement of civil society, human rights and equity, and adaptation to the unique context of diverse epidemics and settings**.**

TB and Poverty

The World Bank estimates that there are almost 1.2 billion people living on less than $1 per day. A study conducted by the World Bank, entitled "Voices of the poor", and highlighted the multi-dimensional nature of poverty. The study suggested that poverty includes a lack of material, well-being, absence of infrastructure, lack of power and voice, and an unraveling of social structures.

Further, World Health Organization estimates that approximately one-third of the world's population is infected with tuberculosis (TB). Globally, low and lower middle income countries (i.e. annual GNP per capita less than US$2995) account for more than 90% of TB cases and deaths. About 76% of the world's populations live in these countries. Low income countries (i.e. annual GNP per capita less than US$755) account for 65% of TB cases and 71% of deaths, about 42% of the world's population live in these countries. Tuberculosis can drive entire countries, not just the people within them, into ever deeper poverty.

The Cycle of TB and Poverty

TB is a disease of poverty, an estimated 95% of new TB cases and 98% of all TB deaths are in the developing world, with more than half of all deaths occurring in Asia. The risk of becoming infected with TB is associated with malnutrition, crowding, poor air circulation, and poor sanitation – all factors associated with poverty.

Even when TB services are free of charge, the disease is costly to the poor. The average TB patient loses three to four months of work time and up to 30% of their yearly household earnings. Families may be forced to sell what little livestock or land they have.
The poverty cycle worsens as children are forced to quit school as there is no money for uniforms or fees, or because they have to work to support the family. In this manner, poverty is passed on from generation to generation.

"TB is the child of poverty – and also its parent and provider." – Archbishop Desmond Tutu

Challenges and Barriers that Hinder Patients Access to TB Treatment

Poor people with tuberculosis (TB) face huge barriers in accessing TB testing and treatment services. If TB control is to be effective, they need quicker diagnosis and treatment options as close as possible to their homes. Findings show that people living in poor communities tend to have limited knowledge about TB and experience a variety of barriers preventing them from accessing proper diagnosis and treatment. Gender, age, socio-economic status and geographical location intertwine with poor and ineffective health systems to create serious challenges for TB control.

Poverty affects people's ability to access services at all stages of care-seeking: from symptoms, to help seeking, health services, diagnosis, treatment adherence and a final positive outcome. Poor people need to have these barriers which prevent them from accessing services removed. Pro-poor approaches should include a range of measures to improve the geographical, economic and social access to TB services.

Economic barriers – there is a complex pathway to care for poor people

Geographical barriers – distance from services providing TB diagnosis and treatment

Socio-cultural barriers – stigma and lack of knowledge of TB and available TB services

Health system barriers – lack of health system responsiveness

Overcoming Barriers to TB Treatment

Kenya's Constitution 2010, Chapter 4 under the Bill of Rights, Article 43 guarantees fundamental social and economic rights to its people. These include;

- 43: 1 (*a*) to the highest attainable standard of health, which includes the right to health care services, including reproductive health care;
- 43:1 (*c*) to be free from hunger, and to have adequate food of acceptable quality;
- 43:1 (e) to social security; and
- 43: (3) The State shall provide appropriate social security to persons who are unable to support themselves and their defendants.

The above mentioned rights are assertive and bind the state giving rise to social protection schemes such as; a) National Health Insurance Fund (NHIF) mandated to provide health provide accessible, affordable, sustainable and quality health insurance for all Kenyan citizens who have attained the age of 18yrs and a monthly income of KES1,000 and above. This may be easy to most Kenyans but difficult to TB patients who may have lost employment while on the long treatment /not having any form of income. NHIF does not have any exclusion criteria, such as pre-existing conditions.

The constitution prevents discrimination on its citizens;
27(4) The State shall not discriminate directly or indirectly against any person on any ground, including race, sex, pregnancy, marital status ,health status, ethnic or social origin, colour, age, disability, religion, conscience, belief, culture, dress, language or birth

The Government of Kenya protects Persons Living with Disability as spelt out in the disability act 2003; to provide for the rights and rehabilitation of persons with disabilities; to achieve equalization of opportunities for persons with disabilities; to establish the National Council for Persons with Disabilities; and for connected purposes. Disability in this case is defined as a physical, sensory, mental or other impairment, including any visual, hearing, learning or physical incapability, which impacts adversely on social, economic or environmental participation. Most of the leprosy and drug resistant TB survivors end up in this category at the completion of treatment.

There are a range of approaches that could be applied to make TB services more accessible to poor people, otherwise TB will remain uncontrolled among the very people who need TB control the most.

- Decentralization of TB treatment diagnostic services
- Patient support(enablers and incentives) program: addressing food security -Nutritional support could include nutritional counseling, cash transfers and subsidizing food costs and/or food vouchers
- Baseline and follow up investigations and transport support all TB and Leprosy

Poor Health Systems

Even when people are able to overcome the barriers to accessing help for their TB, the quality of health systems varies widely throughout the world due to a number of challenges including:

- Limited financial resources
- Insufficient numbers of healthcare professionals
- Poor infrastructure
- Inequality in the provision of services
- A lack of high-quality drugs and diagnostics
- A lack of community participation in planning services

ANNEXES

ANNEX 1:

PROCEDURE FOR OBTAINING SPUTUM SAMPLES FOR MICROBIOLOGY THROUGH GASTRIC ASPIRATION

Background

Children with TB may swallow mucus which contains M. tuberculosis. Gastric aspirates are used for collection of samples for GeneXpert, microscopy and mycobacterial cultures in young children suspected of having pulmonary TB when sputa cannot be spontaneously expectorated nor induced using hypertonic saline. GeneXpert and culture enable the determination of the susceptibility of the organism to anti-TB drugs. Microscopy can sometimes give false-positive results (especially in HIV-infected children who are at risk of having non-tuberculous mycobacterium).

During sleep, the lung's mucociliary system beats mucus up into the throat. The mucus is swallowed and remains in the stomach until the stomach empties. Therefore, the highest-yield specimens are obtained first thing in the morning. Gastric aspiration on each of three consecutive mornings should be performed for each patient. This is the number that seems to maximize yield of smear- positivity. Of note, the first gastric aspirate has the highest yield.

Performing the test properly usually requires two people (one doing the test and an assistant). Children not fasting for at least 4 hours (3 hours for infants) prior to the procedure and children with a low platelet count or bleeding tendency should not undergo the procedure.

The following equipment is needed:

- Gloves
- Nasogastric tube (usually 10 French or larger)
- 5, 10, 20 or 30 cm^3 syringe, with appropriate connector for the nasogastric tube
- litmus paper specimen container
- Pen (to label specimens)
- Laboratory requisition forms
- Sterile water or normal saline (0.9% NaCl) Sodium bicarbonate solution
- (8%) Alcohol/chlorhexidine.

Procedure

The procedure can be carried out as:

- An inpatient: first thing in the morning when the child wakes up, at the child's bedside or in a procedure room on the ward (if one is available), or as
- An outpatient (provided that the facility is properly equipped). The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

1. Find an assistant to help.
2. Prepare all equipment before starting the procedure.
3. Position the child on his or her back or side. The assistant should help to hold the child.
4. Measure the distance between the nose and stomach, to estimate distance that will be required to insert the tube into the stomach.
5. Attach a syringe to the nasogastric tube.
6. Gently insert the nasogastric tube through the nose and advance it into the stomach.
7. Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
8. To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This can also be checked by pushing some air (e.g. 3–5 ml) from the syringe into the stomach and listening with a stethoscope over the stomach.)
9. If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again.

   If still unsuccessful, attempt this again (even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small).

   Do not repeat more than three times.
10. Withdraw the gastric contents (ideally at least 5–10 ml).
11. Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
12. Add an equal volume of sodium bicarbonate solution to the specimen (in order to neutralize the acidic gastric contents and so prevent destruction of tubercle bacilli).

After the procedure

1. Wipe the specimen container with alcohol/chlorhexidine to prevent cross-infection and label the container.
2. Fill out the laboratory requisition forms.
3. Transport the specimen (in a cool box) to the laboratory for processing as soon as possible (within 4 hours).
4. If it is likely to take more than 4 hours for the specimens to be transported, place them in the refrigerator (4–8 ˚C) and store until transported.
5. Give the child his or her usual food.

Safety

Gastric aspiration is generally not an aerosol-generating procedure. As young children are also at low risk of transmitting infection, gastric aspiration can be considered a low risk procedure for TB transmission and can safely be performed at the child's bedside or in a routine procedure room.

ANNEX 2:
HOW TO PERFORM A TUBERCULIN SKIN TEST

A Tuberculin Skin Test (TST) or Mantoux test is the intradermal injection of a combination of mycobacterial antigens which elicit an immune response (delayed-type hypersensitivity), represented by in duration, which can be measured in millimeters. The TST using the Mantoux method is the standard method of identifying people infected with M. tuberculosis. Multiple puncture tests should not be used to determine whether a person is infected, as these tests are unreliable (because the amount of tuberculin injected intradermally cannot be precisely controlled).
Details of how to administer, read and interpret a TST are given below, using 5 tuberculin units (TU) of tuberculin PPD-S. An alternative to 5 TU of tuberculin PPD-S is 2 TU of tuberculin PPD RT23.

Preparation

When preparing to administer the Mantoux tuberculin skin test, make sure that the area for administering the test has a firm, well-lit surface, and that equipment and supplies are ready.

Supplies should include a vial of tuberculin, a single-dose disposable tuberculin syringe, one-quarter to one-half inch, 27-gauge needle with a short bevel, a ruler with millimeter (mm) measurements, 2x2 gauze pads or cotton balls, alcohol swabs, a puncture-resistant sharps disposal container, record-keeping forms for the patient and provider, and a pen.

To avoid reducing the potency of the tuberculin, store it inside a refrigerator so that it remains between 35 and 46 degrees Fahrenheit or between 2 and 8 degrees Centigrade.

Also store and transport the tuberculin in the dark as much as possible and avoid exposure to light.

Discuss with the patient why the skin test is given, what is involved in the procedure, and when the patient should return for the test to be read. If a patient can't return within the 72-hour time period, do not administer the test. Instead, schedule another time that allows the patient to come for both the test and the return appointment.
It's also important to encourage the patient to ask questions and talk about any anxieties he or she may have about the test. That way you can answer any questions and ease any fears the patient may have. After providing patient education, you should wash your hands, using an appropriate hand-washing technique, before administering the test or any other procedure involving patient contact.

Administration

1. Locate and clean injection site 5–10 cm (2–4 inches) below elbow joint

Place the forearm palm-side up on a firm, well-lit surface.
Select an area free of any barriers to placing and reading the skin test such as muscle margins, heavy hair, veins, sores, or scars.

Clean the area with an alcohol swab by circling from the center of the site outward. Allow the site to dry completely before the injection. Because some of the tuberculin solution can adhere to the inside of the plastic syringe, the skin test should be given as soon as possible after the syringe is filled.

2. Prepare syringe

Look at the vial label to make sure the vial contains tuberculin PPD-S (5 TU per 0.1 ml) and expiration date.

When you open a new vial, write the date and your initials on the label to indicate when the vial was opened and who opened it.
Fill the syringe with 0.1 ml tuberculin.

3. Inject tuberculin (see Figure 3)

The Mantoux tuberculin skin test is an intradermal injection.

With the needle bevel against the patient's skin, insert it slowly at a 5 - 15 degree angle. The 5- 15 degree angle is very important because this layer of skin is very thin.

For an intradermal injection, the needle bevel is advanced through the epidermis, the superficial layer of skin, approximately 3 mm so that the entire bevel is covered and lies just under the skin. The injection will produce inadequate results if the needle angle is too deep or too shallow.

When the needle is inserted at the correct angle you can see the bevel of the needle just below the skin surface. Next, release the stretched skin and hold the syringe in place on the forearm.

Now, slowly inject the tuberculin solution. You should feel fairly firm resistance as the tuberculin enters the skin. A tense, pale wheal that's 6 to 10 mm in diameter appears over the needle bevel. Remove the needle without pressing or massaging the area.

Discard the used syringe immediately in the designated puncture-resistant container.

4. Check injection site

After injection, a flat intradermal wheal of 6–10 mm diameter should appear. If not, repeat the injection at a site at least 5 cm (2 inches) away from the original site.

In case a drop of blood appears at the injection site, lightly blot the blood away with a gauze pad or cotton ball.

Do not cover the site with an adhesive bandage because the adhesive could cause irritation and interfere with the test.

Immediately and thoroughly wash your hands.

5. Record information

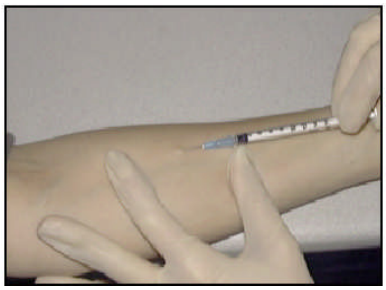
Write the date and the time the test was administered, the name and manufacturer of the injected solution, the lot number, the tuberculin dose administered, the expiration date, the forearm or alternative site in which the injection was given, the site location if you repeat the test, the name of the person who administered the test, and the reason for giving the skin test.

Remind the patient to return

Explain how to care for the injection site after the test. Tell the patient to avoid scratching the site, keep the site clean and dry, and avoid putting creams, lotions, or adhesive bandages on it. Also mention that getting the site wet with water is not harmful, but the site should not be wiped or scrubbed.

Return the tuberculin vial to the refrigerator, or other cooling container.

Administration of the Tuberculin Skin Test



Reading

The results should be read 72 hours after administration. A patient who does not return within 72 hours will probably need to be rescheduled for another TST.
Have a small, plastic, flexible ruler marked in millimeters to measure the test, a pen to mark the edges of the induration, and an alcohol pad to clean off the pen marks. You'll need the patient's record or other appropriate forms for documenting the measurement results.

1. Inspect site

Visually inspect injection site under good light and on a firm surface.

Use fingertips to find the margins of induration which is a hard, dense, raised formation. This is the area that is measured. Sometimes the site has erythema, a reddening of the skin that can also have swelling. The erythema should NOT be measured.

Mark induration.

2. Measure diameter of induration using a clear flexible ruler

The diameter of the induration is measured across the forearm; from the thumb side of the arm to the little finger side of the arm or vice versa.

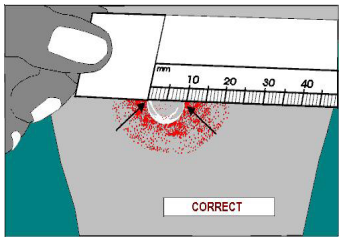
Place "0" of ruler line on the inside-left edge of the induration.

Read ruler line on the inside-right edge of the induration (use lower measurement if between two gradations on mm scale).

3. Record diameter of induration

Do not record as "positive" or "negative". Only record the measurement in millimeters. If no induration, record as 0 mm.

Reading the Tuberculin Skin Test



Interpretation

TST interpretation depends on two factors:

- Diameter of the induration.
- Person's risk of being infected with TB and risk of progression to disease if infected.

Mantoux is positive if induration is:

- 10mm in a well-nourished, HIV negative child
- 5mm in a malnourished, or HIV infected child

A negative mantoux does not rule out TB infection or disease (especially in the HIV positive or malnourished child).

ANNEX 3:

ADULT & ADOLESCENT DOSAGES FOR SECOND LINE ANTI TB MEDICINES

Drugs	Weight Class			
	Average daily dosing	33-50kg	51-70kg	>70kg
Isoniazid (H) (100,300 MG)	10-20 mg/kg daily	200 - 300 mg daily	300mg daily or	300mg
Rifampicin ® (150, 300m mg)	10-20 mg/kg daily	450-600 mg	600 mg	600 mg
Ethambutol (E) (100, 400 mg)	25 mg/kg daily	800-1200 mg	1200-1600 mg	1600-2000 mg
Pyrazinamide (Z) (500 mg)	30-40 mg/kg daily	1000-1750 mg	1750-2000 mg	2000-2500 mg
Streptomycin (S) (1 G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Kanamycin Km (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Amikacin (AM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Capreomycin (CM) (1G vial)	15-20mg/kg daily	500-750 mg	1000 mg	1000 mg
Ofloxacin (Ofx) (200,300,400mg)	The usual adult dosefor MDR-TB is 800 mg	800 mg	800 mg	800-1000 mg
Levofloxacin (LFX) (250,500 mg)	The usual adult dose for MDR-TB is 750 mg	750 mg	750 mg	750-1000 mg
Moxifloxacin (Mfx)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Gatifloxacin (Gfx) (400 mg)	The usual adult dose for MDR-TB is 400 mg	400 mg	400 mg	400 mg
Ethionamide (Eto) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Prothionamide (Pto) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Cycloserine (Cs) (250 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
Terizidone (Trd) (300 MG)	15-20 mg/kg daily	500 mg	750 mg	750-1000 mg
PAS 4gm sachets	150mg/kg daily	8gm	8gm	8-12gm

The drugs are administered once a day for six days per week. Each dose is given as directly observed therapy throughout the course of treatment.

ANNEX 4:

PEDIATRIC DOSAGES FOR SECOND LINE ANTI TB MEDICINES

Medication	Dose	Maximum daily dose
Isoniazid(H)	10mg/kg daily	300mg
Rifampicin (R)	15mg/kg daily	600mg
Ethambutol (E)	25mg/kg daily	1200mg
Pyrazinamide (Z)	30 -40 mg/kg daily	1500mg
Streptomycin (S)	20 - 40mg/kg daily	1000mg
Kanamycin (K)	15 -30mg/kg daily	1000mg
Capreomycin (Km)	15 -30mg/kg daily	1000mg
Ofloxacin (Ofx)	15 - 20mg/kg daily	800mg
Levofloxacin (Lfx)	15 - 25mg/kg daily	1000mg
Moxifloxacin (Mfx)	7.5 -106mg/kg daily	400mg
Ethionamide (Eto)	15 – 20 mg/kg daily	1000mg
Cycloserine (Cs)	10 – 20mg/kg daily	1000mg
Terizidone(Trd)	10 – 20mg/kg daily	1000mg
Para – aminosalisylic acid (PAS)	150mg/kg daily	8g(PASER)

ANNEX 5:

SIDE-EFFECTS FOLLOW-UP FORM

Document the treatment being used – drug(s) and dosages

Name:	Current treatment regimen – drugs and dosages:					
Week of treatment						
Date						
Sweats						
Cough						
Abdominal pain						
Constipation						
Nausea						
Vomiting						
Anorexia						
Diarrhoea						
Headache						
Periph neuro						
Hypothyroidism						
Low magnesium						
Low potassium						
Skin rash						
Itching						
Joint pain						
Dizziness						
Vision loss						
Hearing loss						
Psychosis						
Convulsions						
Others						

ANNEX 6:

ADMINISTRATIVE CONTROL MEASURES FOR SUB COUNTY AND COUNTY REFERRAL HEALTH CARE FACILITY

Sub County level measures (community networks, dispensaries, health centers, and hospitals)	**County Referral level measure** These additional measures apply to referral-level facilities
Identification of the person(s) responsible for the assessment, implementation and monitoring of TB-IC plan	Identification of the person(s) or team – such as the IC team who would be responsible to assist in the assessment, the implementation and monitoring of TB-IC plan
Assessment of at-risk settings for acquiring *M. tuberculosis* infection	* When medically allowable, encourage out-patient TB management
TB Infection, prevention and Control Plan	*In-patient management and isolation policies
HCW training and TB awareness	*Isolation of multidrug-resistant (MDR) and extensively drug resistant TB (XDR- TB) as long as cultures are positive
Access to HIV C&T	*Enforcing isolation policies
Early identification and diagnosis	*Special Areas and Topics in Infection, prevention and Control: Radiology, Sputum collection and cough-inducing procedures, bronchoscopy suites, surgical suites, intensive care areas, Immuno-suppression and TB
Patient education	Evaluating infection control interventions, Surveillance for TB, disease/infection among HCWs
Sputum collection	
Triage and evaluation of presumptive TB	
Flowchart path of inpatients and outpatients, including functional procedures	
Flowchart path of specimens.	
TB patients in the health post or clinic	
Reducing exposure in the laboratory	
Evaluating infection control interventions	

Surveillance for TB, disease/infection among HCWs

*** should be implemented at the Sub County hospital facilities**

ANNEX 7:

SAMPLE OF INFECTION PREVENTION AND CONTROL PLAN

A. The plan will include, but not be limited to, the following policy areas:

1. Identification of responsible coordinators at all levels for the implementation IC plan.
2. Screening patients to identify persons with symptoms of TB disease or who report being under investigation or treatment for TB disease. Carry out contact tracing of sputum positive PTB including MDR-TB and XDR-TB.
3. Providing face masks or tissues to persons with symptoms of TB disease ("presumptive TB") or who report being under investigation or treatment for TB disease ("Presumptive TB or cases"), and providing waste containers for disposal of tissues and masks.
4. Placing Presumptive TB and cases in a separate waiting area.
5. Triaging Presumptive TB and cases to the front of the line to expedite their receipt of services in the facility.
6. Referring Presumptive TB to TB diagnostic services and confirming that TB cases are adhering with treatment.
7. Using and maintaining environmental control measures.
8. Educating staff periodically on signs and symptoms of TB disease including Multidrug resistant TB , specific risks for TB for HIV-infected persons, and need for diagnostic investigation for those with signs or symptoms of TB.
9. Training and educating staff on TB control, and the TB infection prevention and control plan.
10. Sensitizing and educating the community on TB disease, TB infection prevention and control.
11. Adequate budgeting and timely implementation of the activities.
12. Monitoring and evaluation of the TB infection and control implementation plan.

B. The facility will implement each policy by following the procedure(s) that accompany it.

Policy 1: Screening patients to identify persons with symptoms or recent history of TB disease.

Procedures:

1. Before patients enter an enclosed part of the facility, a designated staff person should ask each adult and any child capable of coughing forcefully (usually age 14 or older) about symptoms or recent history of TB. The questioning should occur before patients wait in line for long periods to register or obtain services.

2. A combination of symptoms have been recommended as sensitive and specific for TB. A simple screen is

   "Do you have a cough?" *If patient answers" yes," ask*

   "For how long have you been coughing?"

   An adult who has had cough for two weeks or more may be considered a TB presumptive TB .

   To determine whether a patient may be under investigation or a diagnosed case of TB, who may still be infectious, ask

   "Are you being investigated or treated for TB?"

3. Classify the as presumptive TB case if he answers yes.
4. Staff seeing patients in examination rooms should any presumptive TB case to the infection control officer in a timely manner so that factors contributing to the potential exposure (e.g., an emergency or short staffing interfering with the designated person screening all patients) can be documented and corrected.

Policy 2: Instructions on cough hygiene

Procedures:

1. Patients who are found to be Presumptive TB or cases should immediately be informed about the importance of cough hygiene and are handed tissues (or pieces of cloth) and instructed to cover their mouths and noses when they cough. Alternatively, patients should be given a face mask, and asked to wear it while in the facility. Patients should also be instructed to dispose of used tissues or masks in identified no-touch receptacles and not on the ground. When tissues, cloths or face masks are not available, clients should be instructed to lift their arm up and cover their nose and mouth with the inner surface of the arm or forearm when they cough or sneeze. *M. tuberculosis* cannot be spread from the hands, but other serious lung infections can.
2. No-touch receptacles for disposal of used tissues and masks should be available in the waiting areas.
3. Advised to wash their hands with soap before leaving.

Policy 3: Placing Presumptive TB and cases in a separate waiting area

Procedures

1. A staff person should direct or escort the patient to a separate waiting area. This special waiting area should have the highest natural ventilation possible. Patients should be assured of their place in the line for registration and/or services.

Policy 4: Triaging Presumptive TB and cases to the head of the line to receive services in the facility

Procedures

1. Presumptive TB and cases should be moved to the front in the queue of the line for whatever services they want or need, e.g., VCT, medication refills, or medical investigation. This reduces the duration of potential exposure while they wait in the facility and may be an incentive to disclose information during screening.
2. Other points should be explained about this procedure/policy.

Policy 5: Referring Presumptive TB to TB diagnostic services

Procedures

1. _____ is the designated staff person to counsel patients about obtaining TB diagnostic services.
2. Patients will be referred to_____ (TB diagnostic center the HIV care facility has a previously negotiated agreement, see section).
3. Patients should be given a card with the name, location, and operating hours of the TB diagnostic center. The card should also have the name of the referring facility on it, with date of referral marked. These cards can be collected at the TB center and used as an anonymous check on number of referrals who successfully obtain TB services. (See also the Presumptive TB and case form listed in Annex A2, which can be used to cross-reference referrals that are made /successful).

Policy 6: Using and maintaining environmental control measures

Procedures

1. _____ is the designated staff person to check on environmental control measures and maintain a log of monitoring and maintenance.
2. Windows and doors should be checked on a daily basis to assure they are in proper position (open or closed as called for in the plan). Generally, all windows and doors should be open when natural ventilation is the primary environmental control to allow for the free, unencumbered movement of air (e.g., across room, from window to door or vice versa). Generally, all windows and doors should be closed when using mechanical ventilation to ensure air movement in a controlled manner (air from supply vent and from slots either under or in door toward the exhaust vent).
3. Fans should be checked on a monthly basis to assure they are clean, are pulling (or pushing) the correct amount of air, and are pulling (or pushing) air in the correct direction.

Policy 7: Providing confidential TB and HIV services to health care workers and staff

Procedures

1. Health care workers and all other staff working at the facility should be educated about the signs and symptoms of TB and encouraged to seek investigations promptly if they develop symptoms and signs suggestive of TB.
2. Health care workers and other staff should be informed about the special specific risks for TB for HIV-infected persons (see section on Training of staff).
3. Health care workers and staff should be encouraged to undergo HIV testing, and given information on relevant HIV care resources.
4. Staff training should include reduction of stigma of TB and HIV
5. _____is responsible for determining when staffs who develop TB disease may return to work and their deployment.
6. Staff who develop TB disease may return to work when determined to be no longer infectious after:

a. Having completed at least two weeks of standard anti-TB therapy
b. Exhibiting clinical improvement; and
c. Having continued medical supervision and monitoring of treatment until cured
d. Where possible, having had three consecutive negative sputum smears obtained on three different days with at least one morning specimen. (Note: Frequent evaluation of sputum smear status may not be done routinely in resource-limited settings.)

Policy 8: Training of staff on all aspects of TB and the TB infection control plan

Procedures

1. _____ is the designated staff person to provide training to new staff as it is hired and to maintain a log indicating who has had initial training.
2. _____ is the designated staff person to provide annual training to all staff and to maintain a log indicating who has attended training. This may be incorporated into a broader training topic or be stand-alone TB infection control training.

Policy 9: Monitoring the TB infection control plan's implementation

Procedures

1. Determine the frequency of the infection control plan
   a. During initiation of procedures, monitoring and evaluation should be done frequently, perhaps monthly or bi-monthly.
   b. When procedures are running well, less frequent evaluation will be necessary at a minimum, annually.
2. Evaluate the screening process
   a. Were patients with significant cough missed when entering the facility and only detected at a later time or in the examination room?
   b. What correctable factors were associated with these potential exposures?
3. Evaluate the success of referrals to the TB diagnostic center
   a. Did referred patients access care?
   b. Did referred patients have TB disease?
   c. What changes in screening or referral process should be made, if any?
4. Evaluate the training process
   a. Did all new staff receive training on TB infection control during their induction?
   b. Did all staff receive annual re-training on TB infection control?
5. Revise the infection control plan to reflect changes in staff responsibilities, policies, and procedures.
6. Develop a plan for correcting inappropriate practices or failure to adhere to institutional policies
   a. Identify incentives to participate fully and adhere to policies.
   b. Identify corrective actions if policies are not followed.

ANNEX 8:
SAMPLE MONITORING TOOLS

_____ has the responsibility for overseeing the evaluation of the TB infection, prevention and control policies and its procedures, and reports to (*Head of the NTLD UNIT*, *Sub County health executive committee, etc).*

_____ has the responsibility for filling out the "TB case and presumptive TB log" on a daily basis, entering the date, names of patients who were found to be a case or presumptive TB that day, whether they were missed at intake screening, and to which facility they were referred.

_____ has the responsibility for conducting follow up on patients referred to a TB diagnostic facility and recording the outcomes of their investigation in the log.

_____ has the responsibility to summarize and present the results of the screening process to relevant management and staff periodically.

TB Case and Presumptive TB Log

Date	Patient Name	Case or Presumptive TB (c/s)	Missed at intake?* (y/n)

*Missed at intake = symptoms or history detected only after patient enters private room with clinician or counselor instead of upon entry to the facility; or after numerous visits while symptomatic yet undetected: y=yes, n=no

**Outcomes: TB diagnosed or confirmed=TB; TB ruled out after diagnostic investigation=not TB; did not present to referral facility for investigation=NS (not seen).

Staff TB Infection, prevention and Control Training Log

Staff Name	Start Date	Date first IC training	Date annual training	Date annual training	Date annual training

ANNEX 9:

TB INFECTION, PREVENTION AND CONTROL ASSESSMENT

- The purpose of this survey is to assess:

  The extent to which infection control policies and guidelines exist

  Knowledge and practices related to basic TB infection control measures.
- The assessment is targeted to both NTLD UNIT and NASCOP program staff.
- The results will be analyzed to identify areas in which additional technical assistance is needed for TB/HIV program implementation.

A summary of results and recommendations will be shared with the in-country CDC team.

National Level

1	Question	Response or Code	Additional Comments
1	**Country:** **Name of Respondent:** **Respondent Title:** **Program: Circle one: NTLD** **UNIT: NAP** **Date Form Completed (dd/mm/yyyy):**		
2	How many administrative Sub Countys currently exist?		
3	Is there a designated national TB/HIV coordinating committee? (0=No, 1=Yes)		
4	Does the **NTLD UNIT** national manual address TB infection, prevention and control? (0=No, 1=Yes)		
5	Is there a written national policy that addresses TB infection control? (0=No, 1=Yes) If yes, describe it (who developed? Target audience? Status of implementation?)		
6	Has this national policy been disseminated? (0=No, 1=Yes)		
7	Has training on implementation of this national policy been conducted? (0=No, 1=Yes)		
8	Has the implementation of this national policy been evaluated? (0=No, 1=Yes)		
9	Request copy of most recent annual report/statistical profile.		

Sub County Level

	Question		Response or Code	Additional Comments
1	**Sub County:** **Name of Respondent:** **Respondent Title:** **Date Form Completed (dd/mm/yyyy):**			
2	What is the total number of TB clinic sites in the Sub County?			
3	How many TB patients were reported in the last quarter? Last year quarter? Sub County population:		Qtr### Yr ###	
4	What is the total number of HIV care and treatment sites providing ARV treatment in the Sub County?			
5	Do HIV care and treatment sites in the Sub County screen patients for active TB? (0=no, 1=yes) If YES, how? Obtain pt encounter from.			
6	How many of the TB sites and HIV care and treatment sites are co-located? Describe co-location			
7	Is there a Sub County-level TB/HIV coordinator? (0=No, 1=Yes)			
8	Has training on TB infection control been provided…? (0=no, 1=yes)	9.1 For staff in HIV care and treatment programs 9.2 For staff in TB clinics 9.3 For staff in Hospitals		
9	Is there a Sub County policy on TB infection control? (0=No, 1=Yes) If yes, request a copy.			
10	Do facilities in the Sub County report on the number of TB cases among HCWs in the Sub County? (0=No, 1=Yes) If yes, request a copy.			

FACILITY-LEVEL

Facility name:.....

Province / Sub County: .....

Name of person administering the interview:.....

Title of respondent: .....

Program (circle one): TB Program HIV/AIDS care/Rx

Date form completed (dd/mm/yyyy): _____ / _____ / _____

Period of time covered by evaluation: _____ / _____ / _____ **to** ____

/ _____ / _____

	Question	Response or Code	Additional comments
General information			
1	Type of facility? (1. Ministry of public health & sanitation, 2. NGO (including faith-based), 3. other)		
2	Type of facility? (0=TB service clinic in primary health center, 1=TB clinic in a hospital, 2=TB clinic (standalone) 3= Out-Patient Department (OPD) clinic, 4=HIV care and treatment site 5=In-patient ward 6= Other)		
3	Does this facility have a designated infection control officer? (0=no, 1=yes)		
4	How many full time staff works at this clinic? (Doctors, nurses, counselors, pharmacists, cleaners etc)?		
5	How many part time staff works at this clinic? (Doctors, nurses, counselors, pharmacists, etc)?		
6	In the last year, how many staff members were diagnosed with TB?		

Administrative (workplace)			
1	Has a facility risk assessment been conducted? (0=no, 1=yes)		
2	Does this facility have a written infection control policy?(0=no, 1=yes) (if yes, OBTAIN a copy)		
3	What training has staff received on TB infection control?		

4	Are staffs screened for TB? If yes, how?(0=no, 1=yes)		
5	Are staffs offered confidential HIV counseling and testing? (0=no, 1=yes)		
6	At peak time, describe the waiting area? What is the estimated waiting time from registration until seen by a nurse? (## min/hr)		
7	What procedures are in place to identify patients observed to have chronic cough and to fast-track to diagnosis? "Cough officers?"		
8	Are clients observed with chronic cough isolated in separate room or outside while waiting to see a nurse/doctor? (0=no, 1=yes)		
9	Describe education procedures in-place for cough hygiene for TB presumptive TB /patients.		
10	Are posters displaying cough hygiene prominently displayed? (0=no, 1=yes)		
11	Review the path of the patient. Identify bottlenecks such as crowded interior waiting rooms, evaluate time separation & space separation, etc.		
12	HIV care and treatment sites: Do you screen patients for active TB? (0=no, 1=yes) If YES, how? Obtain pt encounter from.		
13	What is the sputum turn-around time for specimens collected on presumptive TB ? (## days)		
14	In-patient: Describe any cohort nursing practices observed.		
Respiratory Protection			
1	Are surgical masks or tissue paper available for coughing patients who cannot be separated? (0=no, 1=yes)		
2	Are NIOSH or CEN-rated respirators available for staff? If yes, describe when they are utilized. (0=no, 1=yes)		
Environmental controls			
1	Describe the natural ventilation: - In the waiting area. - In the consultation room - On the ward (in-patient)		
2	Cross-ventilation for air movement: sketch placement windows and doors		
3	In-patient wards: Are windows kept open at night? (0=no, 1=yes)		
4	Is there electricity at this facility? (0=no, 1= intermittent, 2=yes)		
5	If electricity is available, assess options to increase air mixing via use of fans.		

ANNEX 10:
VENTILATION

Ventilation is the movement of air to achieve dilution and air exchange in a specific area. This process reduces the concentration of airborne droplet nuclei. To reduce nosocomial risk, the most ideal situation would be one in which fresh air is constantly pulled into a room and the contaminated air is exhausted to the outside, such that the air in the room is changed several times every hour (Figure 1).

The most common way in such ventilation can be established is through the use of negative pressure ventilation, in which a room is kept at negative pressure relative to the surrounding area and air is drawn into the room from the corridor and exhausted directly outside. If designed properly, such rooms can be cost- effective. However, the equipment needed requires ongoing maintenance and the air exchange rate may be less that the average air exchange rate from well-designed natural ventilation. More feasible in most settings is the use of natural ventilation or of mechanical ventilation in which the movement of air is facilitated by the use of fans. However, if administrative policies are not in place to ensure windows are open, this environmental control is of minimal effectiveness. Table X shows the time necessary to clear the air of 90%, 99%, and 99.9% of airborne contaminants, in a well-mixed room. The recommended is 12-15 air changes per hour (ACH) designed to achieve 99% effectiveness

Table X. Air changes per hour (ACH) and time required for removal efficiencies of 90%, 99%, an 99.9% of airborne contaminants*

	Minutes required for removal efficiency†		
ACH	90%	99%	99.9%
2	72	138	207
4	36	69	104
6	24	46	69
12	12	23	35
15	10	18	28
20	7	14	21
24	6	12	17
30	5	9	14
40	4	7	10
50	3	6	8
60	2	5	7
70	2	4	6
80	2	3	5
100	1	3	4
200	<1	1	2
400		<1	1

*This table can be used to estimate the time necessary to clear the air of airborne Mycobacterium tuberculosis after the source patient leaves the area or when aerosol-producing procedures are complete. †Time in minutes to reduce the airborne concentration by 90%, 99%, and 99.9%.

HIERARCHY OF VENTILATION

The hierarchy of ventilation for patient areas is:

a. Keep windows/doors open.
b. Enlarge openings to >20% of floor space (>10% on opposing sides).
c. For new construction, design for proper natural ventilation.

d. Well-designed exhaust-only ventilation.

e. Well-design general ventilation (supply and exhaust, no climate control)

f. Well-designed general ventilation (supply and exhaust, with climate control)

a) Natural ventilation

Ventilation is the movement of air in a building and replacement of air in a building with air from outside. Natural ventilation refers to fresh dilution air that enters and leaves a room or other area though openings such as open doors and/or windows. Natural ventilation is controlled when openings are deliberately secured open to maintain air flow. Unrestricted openings (i.e., cannot be closed) on opposite sides of a room provide the optimal natural ventilation. Propeller fans may be an inexpensive way to increase the effectiveness of natural ventilation, by increasing the mixing of airborne TB as well as assisting in the direction of air movement by pushing or pulling of the air.

Natural ventilation is controlled when openings are deliberately secured open to maintain air flow. Unrestricted openings (that cannot be closed) on opposite sides of a room provide the most effective natural ventilation.

Types of propeller fans

Propeller fans include:

- Ceiling fans,
- Small fans that sit on a desk or other surface,
- Fans that stand on the floor, and
- Fans mounted in a window opening

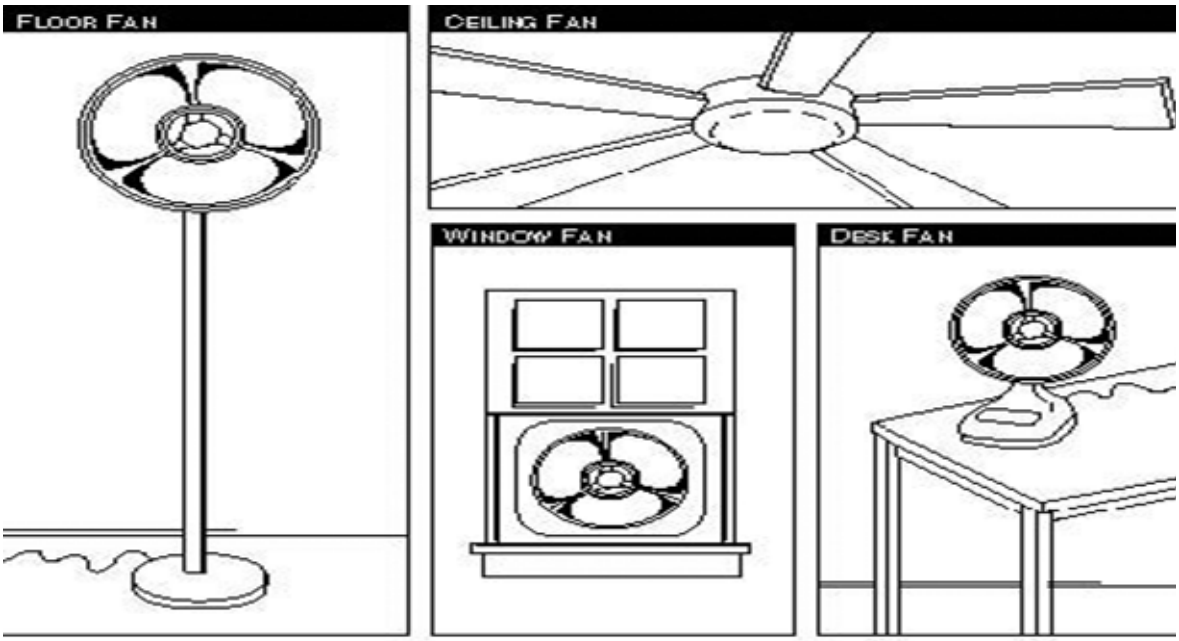


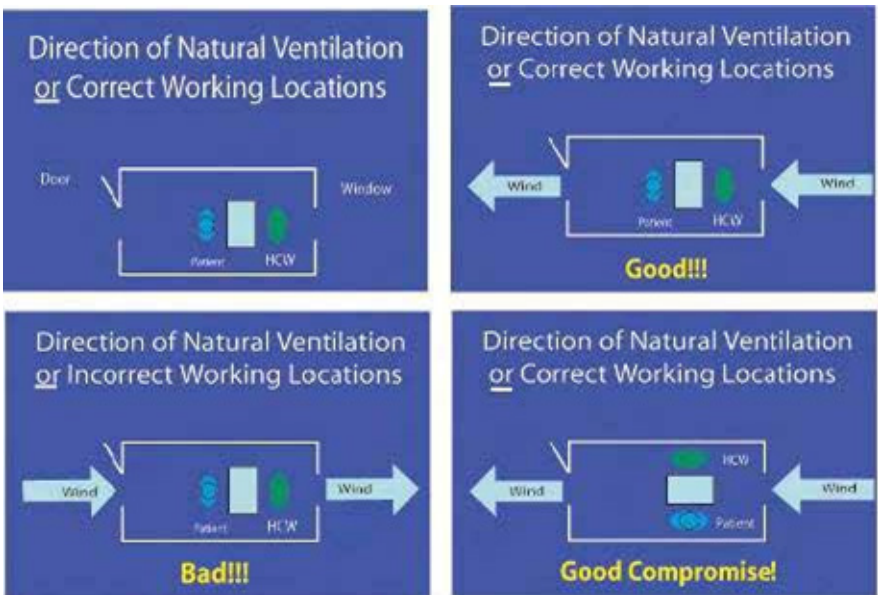
Figure 1. Propeller fans

Air mixing and removal

A propeller fan helps mix air in a room. Mixing of air will reduce pockets of high concentrations, such as in the corners of a room or in the vicinity of patients where natural ventilation alone is not enough. The total number of infectious particles in the room will not change with mixing; however, the concentration of particles near the source will be reduced, and the concentration in other parts of the room may increase.
If this dilution effect is combined with a way to replace room air with fresh air, such as by opening windows and doors, the result will be fewer infectious particles in the room.
A room with an open window, open door, and a fan will have less risk than an enclosed room with no fan, an enclosed room with a fan, or a room with an open window but no fan. In addition, mixing may increase the effectiveness of other environmental controls.

Directional airflow

If placed in or near a wall opening, propeller fans can also be used to enhance air movement into and out of a room. Consider fans installed in the windows or through wall openings on the back wall of a building. The fans exhaust air outside, away from people or areas where air may come back into the building. If doors and windows in the front of the building are kept open, the overall effect should be to draw in fresh air through the front of the building and exhaust air through the rear. Health care staff should be mindful of the direction of airflow to ensure the patient is closest to the exhaust fans and the staffs are closest to the clean air source. This arrangement should done every morning.



With this arrangement, the risk that TB will be spread is greater near the back of the building; however, once the contaminated air is exhausted, dilution into the environment will be fast.

When fresh air enters a room it dilutes the concentration of particles in room air, such as droplet nuclei containing *M. tuberculosis*. Natural ventilation can be used in medical wards or other sites in health facilities in temperate or tropical climates where windows can be left open. Natural ventilation can occur when a room or ward is of open construction with free flow of ambient air in and out through open windows **(Figure 2)**. Maximizing natural ventilation

patterns for the hospital, clinic, ward or room is the simplest approach to achieving better ventilation. Also in temperate or tropical climates, waiting areas should be designed as open-air shelters with a roof to protect patients from sun and rain.

Whenever possible:

Waiting areas, sputum collection areas, examination rooms, and wards should be "open" to the environment (e.g., established in covered open areas or in areas with open windows). Additionally, windows or other openings may be installed that would allow for more ventilation. Windows and openings should be placed on outer walls such that air moves to the outdoors, not into other wards or waiting areas. The open areas should be equal to at least 10% of the area of the room; >20% is preferable. For example, the minimum window opening for a 3m x 5m room (15 m^2) would be a 1.5 m^2 window, door, or other opening on opposing all.

When ceiling fans are used, windows should also be left open since diluting and exchanging of the mixed air is the objective.

The risk of *M. tuberculosis* transmission is greatest in an enclosed room that contains air with aerosolized infectious droplet nuclei. A room with an open window only at one end provides air exchange near the window; however, little air is exchanged a short distance from the window. A ceiling or mixing fan may help increase the overall removal of aerosolized infectious droplet nuclei. Ideally, the minimum acceptable condition is openings on opposite ends of a room (windows, window-door, e.t.c).

b) Mechanical ventilation

In situations where natural ventilation is not feasible or is inadequate, mechanical ventilation can be used to reduce the concentration of infectious droplet nuclei in selected areas or rooms in the health care facility (e.g., patient rooms, waiting rooms, or examination rooms). It is important to use equipment with sufficient power to facilitate air entry into, and exhaust from, the room or area. In other words, if no air is allowed to enter the area, then it will be impossible to exhaust air. It is also important to attempt to direct air movement so that infectious droplet nuclei produced by coughing patients are exhausted *away* from others. Directional air flow should be maintained from a "clean" area, across the HCW, across the patient, and to the outside **(Figure 1)**. The area where air is entering should be located away from the exhaust area to avoid re-entry of contaminated air ("short-circuiting"). Finally, for mechanical ventilation to be acceptable to patients, HCW, and visitors, the air must be tempered (heated or cooled).

Window fans are generally an inexpensive and feasible method of providing mechanical ventilation to direct air flow in many resource-limited settings. However, it is important to ensure that air flows across the room (i.e., under a door and out a window, not in and out the same window or vent). Additional methods of mechanical ventilation, which require more resources, include mechanical exhaust systems that pump clean outside air into the building and then exhaust the contaminated room air back outside. Closed recirculation filtration systems, which take room air, filter it to remove infectious droplet nuclei, and then exhausts it back into the room, are effective but expensive and require considerable maintenance. To create both negative pressure and air exchange, some controlled air leakage into the room is needed. The air leakage could be through a 2-3cm slot under the door or a grill near the bottom of the door. If possible, the efficiency of the air exchange in the room could be enhanced by use of a fan pulling air from the corridor and pushing it into the room. Note that

the flow rate of the fan pushing air into the room should be 90% or less than the flow rate of the fan pulling air from the room and exhausting out-of-doors in order that negative pressure is maintained.

c) Monitoring of ventilation and ventilation systems

Checking natural ventilation

People can usually feel the existence or lack of air movement in a space. A ventilated space has a slight draft. In the absence of ventilation, air will feel stuffy and stale and odors will linger. Use the following checklist to assess natural ventilation in your waiting areas and examination rooms:

- Check air mixing and determine directional air movement in all parts of rooms or areas. One way to visualize air movement is to use incense sticks as described in these six steps.
- Hold two incense sticks together and light them.
- As soon as the incense starts to burn, blow out the flame. Now the incense should produce a continuous stream of smoke.
- Observe the direction of the smoke.
- Observe how quickly the smoke dissipates. This is a subjective test that may require some practice (see figure 2). It does not give a definite result but is useful for comparing one room or area to another.
- Check natural ventilation once a year after the prevailing wind patterns have been determined. Recheck if any changes in the physical environment are made and confirm procedures for ensuring free movement of air are followed.
- Keep records of all routine activities and dates.

Checking fans

- Check that all room fans are working and cleaned once a month. Use cloth or vacuum cleaner to remove dust and lint from fans, grilles, and ducts.
- Check that exhaust fans are working and cleaned once a month. Use cloth or vacuum cleaner to remove dust and lint from fans, grilles, and ducts. Clean ducts behind grilles as far back as can be reached.
- To check fans that have a grille, hold a tissue or piece of paper against the grille. If the exhaust fan is working, the tissue or paper should be pulled against the grille.
- Flow rates through exhaust fans and grilles can be measured using a simple velocity meter and a means to measure that velocity over a known cross-sectional area. The air flow rates can be calculated from simple velocity measurements (see Boxes 1 and 2).
- Air exchange rates (also called air-changes per hour) can be calculated as shown in boxes below. If mechanically ventilating a room, the fan should provide a minimum of six air exchanges per hour.
- Keep records of all routine activities and dates.

Box 1: Estimating air velocity

Measure 0.5 meter distance and mark it on a table top
Move your hand from one end to the other (0.5 meters) in one second. This is equivalent to 0.5 m/s. In order to have directional control of contaminants in air, one should have air moving at least 0.5 m/s.
Example air flow circulation: Fan, duct, or box opening: 0.5m high, 0.5m wide Area = 0.5m x 0.5m = $0.25m^2$ Average air velocity through fan, duct, or box opening: 2.5m/s Average flow rate = Average times $0.25m^2$ x 2.5m/s x 3600s/hour = $2.250m^3$/hour

Box 2: Example air exchange rate calculation

Window opening: 0.5 m high, 0.5 m wide Window area = 0.5 m x 0.5 m = 0.25 m Average air velocity through window: 0.5 m/s Room dimensions: 3 m wide,5 m deep and 3 m high Room volume = 3 m x 5 m x 3 m = 45 m Average flow rate = Area of window times average air velocity.25 m x 0.5 m/sx 3600 s/hour = 450 m /hour Air exchange rate = Average flow rate divided by room volume 450 m /hour÷ 45 m = 10 air exchanges per hour.

Ventilation systems should be evaluated regularly to determine if they are functioning properly. The simplest evaluation includes the use of smoke (e.g., smoke tubes, incense, paper, etc.), a tissue, or a simple vinometer to monitor proper airflow direction. If window fans are being used to produce negative pressure, they should be checked frequently to ensure air movement is directional and is adequate. Evaluations should be documented in a maintenance record.

d) Special areas

Certain areas of the health care facility should be considered high risk and a priority if environmental control measures are implemented. These include TB isolation rooms, TB wards, general waiting areas, or other areas such as intensive care units where TB patients may be housed. Unless natural ventilation is excellent in these areas, mechanical ventilation with window fans to generate directional air flow should be strongly considered. Other high-risk areas may include sputum induction rooms, bronchoscopy suites, operating rooms, radiology, and autopsy suites **(see Table 5.1)**. These areas should be considered high risk before, during and after procedures. Since large rooms may have little or no air movement and may be difficult to ventilate, a smaller, well ventilated room should be considered for bronchoscopy or other high risk procedures. Environmental control measures should only be implemented as a supplement to effective administrative control measures.

Ultraviolet germicidal irradiation (UVGI)

In certain high-risk areas of a facility, use of natural and mechanical ventilation may not be feasible. In these situations, ultraviolet germicidal irradiation (UVGI) or room air cleaners with UVGI may provide a less expensive alternative to more expensive environmental control measures that require structural alterations of a facility. These measures may be particularly useful in larger wards, TB clinic waiting areas or inpatient areas such as television or recreation rooms where TB patients congregate.

Effective use of UVGI ensures that *M. tuberculosis*, as contained in an infectious droplet, is exposed to a sufficient dose of ultraviolet-C (UV-C) radiation at 253.7 nanometers (nm) to result in inactivation. Because dose is a function of irradiance and time, the effectiveness of any application is determined by its ability to deliver sufficient irradiance for enough time to result in inactivation of the organism within the infectious droplet. Achieving a sufficient dose can be difficult with airborne inactivation because the exposure time can be substantially limited; therefore, attaining sufficient irradiance is essential.

Studies show that *M. tuberculosis* is inactivated if the organisms are exposed sufficiently to UVGI. The recommended efficiency is 90% destruction of colony formation. The major concerns about UVGI have been adverse reactions (e.g., acute and chronic coetaneous and ocular changes) in HCWs and patients from overexposure if the UVGI is not installed and maintained properly. If UVGI is to be used, guidelines as well as manufacturer's instructions regarding installation, cleaning, maintenance, and ongoing monitoring should be carefully consulted.

UVGI may be applied in several forms:

- in sputum collection booths, bare bulbs can be used to irradiate the entire booth when it is not occupied
- If HCWs and patients are in the room, continuous upper air irradiation in which shielding placed below the UVGI sources prevents injury to patients but the upper portion of the room is irradiated can be used
- Portable UVGI floor units also may be used
- An additional more expensive option involves the use of UVGI in combination with a closed mechanical system

Continuous upper air irradiation is the most applicable of the above methods in most resource-limited settings. The advantage of this technology is that the upper air is continuously being irradiated; thus, it provides some protection to the HCW while the infectious patient is in the room. Two laboratory studies have shown a reduction by as much as 80% with incomplete air mixing. Thus, to be effective, this technology requires good air mixing to be effective. Furthermore, structural features such as ceiling height may limit the feasibility and usefulness of UVGI. If portable UVGI is used, attention should be paid to lamp placement, since corners may receive inadequate radiation.

The quality of UVGI lamps is very important. Usually a good one will last 5,000 to 10,000 hours (7-14 months). After that, the irradiance may drop off. Responsibility should be assigned to ensure the lamps are cleaned and monitored properly to avoid adverse HCWs and patients' exposure, that air flow patterns maximize *M. tuberculosis* UVGI inactivation, and that UVGI output is adequate. (Maintenance and replacement of Lamps)

Room Air Cleaners

In small rooms with a limited number of patients or in other small, enclosed areas, room air cleaners with HEPA filters may be a useful alternative to mechanical ventilation requiring structural changes or to UVGI. Room air cleaners with HEPA filters may be free-standing or may be permanently attached to floors or ceilings to minimize tampering. If possible, the units can be exhausted outdoors, thereby creating a negative pressure isolation room.

If portable room air cleaners are used, unrestricted airflow is essential; placing the unit close to furniture or putting items on top of the units may compromise their function. Careful regular monitoring is essential.

Room air cleaners with other air-cleaning technologies are commercially available. However, the effectiveness of portable room air cleaners has not been evaluated adequately, and there is probably considerable variation in their effectiveness. HEPA or other filters may also be used in exhaust ducts or vents that discharge air from booths or enclosures into the surrounding room; however, one must ensure that the filters are replaced with identical filters. If a filter other than specified in the original design document is used, the flow rate may be adversely affected. In any application, HEPA or other filters should be installed carefully and maintained meticulously to ensure adequate function. Manufacturers of room-air cleaning equipment should provide documentation of the HEPA or other filter efficiency, or the efficiency of the novel air-cleaning technology, and the efficiency of the installed device in lowering room-air contaminant levels.

High Risk Areas for Nosocomial M. tuberculosis **Transmission**

- **TB patient isolation areas/rooms**
- **Areas/rooms where sputum is collected or induced**
- **Bronchoscopy suites**
- **Surgical suites**
- **Intensive care units**
- **Autopsy suite**

REPUBLIC OF KENYA

MINISTRY OF HEALTH

NATIONAL TUBERCULOSIS, LEPROSY AND LUNG DISEASE PROGRAM

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