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MINISTRY OF HEALTH

INTEGRATED GUIDELINE FOR TUBERCULOSIS, LEPROSY AND LUNG DISEASE

2021

NATIONAL TUBERCULOSIS, LEPROSY AND LUNG DISEASE PROGRAM

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NATIONAL TUBERCULOSIS, LEPROSY AND LUNG DISEASE PROGRAM

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List of Abbreviations

AATD	Alpha-1- antitrypsin
ABC	Abacavir
ABPA	Allergic Bronchopulmonary Aspergillosis
ACCE	Advocacy Communication and Community Engagement
ACE 1	Angiotensin Converting Enzyme
ADRs	Adverse drug reactions
ADR	Adverse Drug Reaction
ADSM	Active TB drug safety, monitoring and management
AE	Adverse events
AFB	Acid Fast Bacilli
AHR	Airway hyper-responsiveness
AIDS	Acquired immunodeficiency syndrome
AKD	Acute Kidney Disease
AKI	Acute Kidney Injury
AP	Antero-posterior view (on chest X-ray)
ARI	Acute Respiratory Infections
ART	Antiretroviral Therapy
ARV	Antiretroviral drug(s)
ATV	Atazanavir
ATV/r	Atazanavir/ritonavir
BCG	Bacillus Calmette-Guerin
BD	Twice daily
BMI	Body mass index
BNP	Brain natriuretic Peptide
CCC	Comprehensive Care Centre
CHV	Community Health Volunteer
CHW	Community Health Worker
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CoK	Constitution of Kenya
CPT	Co-trimoxazole Preventive Therapy
CSF	Cerebrospinal Fluid
CT	Computerized Tomography Scan
CTLC	County TB and Leprosy Coordinator
CTX	Cotrimoxazole
CXR	Chest X-Ray
DALYs	Disability-adjusted life years
DBS	Dried Blood Spot
DM	Diabetes Mellitus
DNA	Deoxyribonucleic Acid
DOT	Directly Observed Therapy
DRT	Drug Resistance Testing
DR-TB	Drug Resistant Tuberculosis
DST	Drug Susceptibility Testing
DS-TB	Drug Sensitive Tuberculosis
DTG	Dolutegravir
EFV	Efavirenz
ENT	Ear Nose and Throat
EPTB	Extrapulmonary Tuberculosis
ESR	Erythrocyte Sedimentation Rate
FBS	Fasting Blood Sugar
FDC	Fixed-dose Combination
FEV	Forced Expiratory Volume
FNA	Fine needle Aspiration
FVC	Forced Vital Capacity
GBV	Gender Based Violence
GERD	Gastroesophageal reflux disease

GFR	Glomerular Filtration Rate
GINA	Global Initiative for Asthma
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HAART	Highly Active Antiretroviral Therapy
HEI	HIV Exposed Infant
HIV	Human Immunodeficiency Virus
HRCT	High Resolution Computed Tomography
ICF	Intensified Case Finding
ICS	Inhaled corticosteroids
IEC	Information, Education and Communication
IGRA	Interferon Gamma Release Assay
ILD	Interstitial Lung Disease
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
IPV	Intimate Partner Violence
IRIS	Immune Reconstitution Inflammatory Syndrome
KHIS	Kenya Health Information System
LABA	Long-acting 2 agonists
LAM	Lipoarabinomannan
LAMA	Long Acting Muscarinic Antagonist
LIP	Lymphoid Interstitial Pneumonia
LLN	Lower limit of normal
LN	Lymph Node
LPA	Line Probe Assay
LPV	Lopinavir
LPV/r	Lopinavir/ritonavir
LRTI	Lower respiratory tract infection
MAM	Moderate Acute Malnutrition
MCG	Micrograms
MDR-TB	Multidrug-Resistant Tuberculosis
MMP-12	Matrix metalloproteinase 12
MRI	Magnetic Resonance Imaging
MTB	Mycobaterium Tuberculosis
MUAC	Mean Upper Arm Circumference
NAAT	Nucleic Acid Amplification Test
NAC	N-Acetylcysteine
NACS	Nutrition assessment, counseling and support
NASCOP	National AIDS and STI Control Program
NGO	Non-Governmental Organization
NHIF	National Hospital Insurance Fund
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitors
NPH	Neutral protamine Hagedorn
NRT	Nicotine Replacement Therapy
NRTI	Nucleoside/Nucleotide Reverse Transcriptase Inhibitors
NSAIDs	Non Steroidal Anti-inflammatory Drugs
NSCLC	Non- small cell lung cancer
NSP	National Strategic Plan
NVP	Nevirapine
OD	Once daily
OGLA	Oral Glucose Lowering Agent
OI	Opportunistic infection
PCP	Pneumocystis Pneumonia
PCR	Polymerase chain reaction
PEF	Peak expiratory flow

PHQ-9	Patient Health Questionnaire 9
PI	Protease Inhibitors
PLHIV	People Living With HIV
PMDI	Pressurised Metered Dose Inhalers
PNS	Post nasal space
PPB	Pharmacy and poison board
PTLD	Post TB Lung Disease
PV	Pharmacovigilance
QF-GIT	QuantiFERON-TB Gold In-Tube Assay
RAL	Raltegravir
RIF	Rifampicin
RMNCH	Reproductive Maternal and Child Health
RSV	Respiratory Syncytial Virus
RTIs	Respiratory tract infections
RTV	Ritonavir
RUTF	Ready to use therapeutic feeds
SABA	Short acting beta agonist
SAEs	Severe adverse events
SAM	Severe Acute Malnutrition
SCLC	Small cell lung cancer
SCTLC	Sub County TB and Leprosy Coordinator
SFP	Supplementary feeding program
SHS	Second Hand Smoke
SLE	Systemic Lupus Erythematosus
SOP	Standard Operating Procedure
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
TPT	Tuberculosis Preventive Therapy
TST	Tuberculin Skin Test
UHC	Universal Health Coverage
UNAIDS	Joint United Nations Programme on HIV and AIDS
VL	Viral load
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant Tuberculosis
3TC	Lamivudine

Foreword

The Division of National Tuberculosis, Leprosy and Lung Disease Program (DNTLD-Program) is mandated to develop policies and guidelines for the management of Tuberculosis (TB), Leprosy and Lung Health in the country. Tuberculosis is a major driver of morbidity and mortality in Kenya affecting all age groups. The burden is greatest among people in the economically productive age group; 25 to 44 years. The country misses over 40% of all TB cases. Kenya is in the post elimination phase of Leprosy however; the Coast and Western regions still report Leprosy cases every year. Major gaps still exist in the detection and management of TB, Leprosy and other lung disease. This guideline seeks to address these gaps by providing evidence-based approaches in the prevention and management of these diseases.

This guideline is a revision of the 2017 Integrated TB, Leprosy and Lung disease guideline. The key thematic areas covered are: Diagnosis and treatment of TB, drug resistant TB and TB in special conditions, nutrition, infection prevention and control, lung health, leprosy, pharmacovigilance and commodity management, community engagement, communication and advocacy. In addition, the 2021 guideline has incorporated novel thematic areas that will improve the quality of care for patients, these include: Active case finding strategies, Latent TB Infection, Human Rights approaches and differentiated care.

The guideline has taken into consideration a patient centered approach towards the management of TB, Leprosy and Lung Disease. It outlines at risk populations for TB and provides evidence-based strategies towards finding the missing people with TB, fronts the use of newer and more sensitive TB diagnostic techniques, incorporates use of the newer shorter-term regimen for treatment of Latent TB infection and provides for individualized care of DR TB patients. With the high burden of TB in the country, the guideline provides for contact management for all contacts of pulmonary bacteriologically confirmed TB patients to ensure they are evaluated and provided with the appropriate treatment.

The goal of this guideline is to provide guidance to the health care workers at all levels on the prevention, diagnosis and management of TB, Leprosy and Lung Disease. It further acts as a reference document for medical students, tutors/lecturers, researchers and the entire community on matters pertaining to TB, Leprosy and Lung Disease.

The mission of the DNTLD program is to accelerate the reduction of TB, Leprosy and lung disease burden through provision of people centered, universally accessibly, acceptable and affordable quality services in Kenya. All efforts should be geared towards attainment of the national targets as provided in the national strategic plan 2019-2023 and the global move towards ending TB.

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

Dr. Patrick Amoth
Ag. Director General,
Ministry of Health

Acknowledgement

The Ministry of Health and the Division of National Tuberculosis, Leprosy and Lung Disease Program (DNTLD-P) sincerely appreciate the invaluable efforts of all the individuals and organizations that contributed to the review of the Integrated Tuberculosis, Leprosy and Lung Disease guideline. The review of this guideline involved extensive deliberations with various stakeholders through consultative meetings and review of existing evidence.

We acknowledge the support from the office of the Cabinet Secretary, the Principal Secretary, Head of Directorate of Medical Services/Preventive and Promotive Health and Head Department of National Strategic Public Health Programs..

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We also appreciate all those who might have contributed in one way or the other but have not been specifically mentioned. Your efforts are recognized and appreciated.

Special gratitude also goes to the peer reviewers who participated in the finalization of the guideline.

Dr. Elizabeth Onyango
Head, Division of National Tuberculosis,
Leprosy and Lung Diseases Program

INTRODUCTION TO THE INTEGRATED GUIDELINE FOR TUBERCULOSIS, LEPROSY AND LUNG DISEASE

1

1.1 Introduction

Respiratory diseases are responsible for a considerable burden of suffering and death in all age groups worldwide. The most frequently occurring respiratory diseases include pneumonias, acute respiratory infections (ARI), tuberculosis (TB), asthma, chronic obstructive pulmonary disease (COPD) and lung cancer.

1.1.1 Tuberculosis

Tuberculosis has existed for millenia and remains a major global health problem. It is an infectious disease caused by a bacillus belonging to a group of bacteria in the mycobacterium tuberculosis complex. Despite it being a preventable and curable disease, Tuberculosis is the leading cause of death due to a single infectious agent. According to WHO, Kenya is one of the 30 high burden TB, TB/HIV and MDR countries in the world. The 2015/2016 Kenya prevalence survey, found an overall national prevalence of 426/100,000 and demonstrated that Kenya misses approximately 40% of people with TB. It also found that, screening for TB using cough of more than two weeks would have missed 52% of the cases. Sixty-seven percent of the prevalent cases with at least one TB related symptom had not sought any health care prior to the survey; majority of whom were men. Among the

Kenya is one of the 30 high burden TB, TB/HIV and MDR countries in the world, According to WHO

426/100,000

Overall national prevalence, according to the 2015/2016 Kenya prevalence survey

40%

Approximate number of people with TB that Kenya misses *(2015/2016 Kenya Prevalence Survey)*

prevalent cases who had sought prior care for their respiratory symptoms, 80% of them had not been diagnosed with TB before the survey. In 2019, Kenya reported 86,504 cases of all forms of TB with 9.7% of all cases notified being children below 15 years of age.

This is the first integrated TB guideline to be produced in the post-2015 era of the Sustainable Development Goals (SDGs) and the End TB Strategy, which have superseded the Millennium Development Goals (2000–2015) and the Stop TB Strategy (2006–2015), respectively. The SDGs were adopted by the UN in September 2015 and cover the period 2016–2030. The End TB Strategy spans a 20-year timeframe (2016–2035) and was unanimously endorsed by WHO's Member States at the 2014 World Health Assembly. The SDGs and the End TB Strategy share a common aim: to end the global TB epidemic. Targets set in the End TB Strategy include a 90% reduction in TB deaths and an 80% reduction in TB incidence by 2030, compared with 2015.

1.1.2 Leprosy

In 1991, the World Health Assembly passed a resolution to "eliminate" leprosy as a public health problem by the year 2000. Elimination, defined as a registered prevalence rate of less than 1 case per 10 000 persons, was realized globally in the year 2000 and in most countries by 2005. This achievement was driven by the utilization of multiple drug therapy (MDT) as a strategy for elimination of leprosy. Kenya is in the post elimination phase of leprosy control, having achieved the WHO elimination target of less than 1 case per 10,000 people in 1989. Despite being in the post elimination phase in leprosy control, Kenya notified 164 leprosy cases in 2019 and increase from 110 in 2018. Majority (90%) of these cases were characterized with multi-bacillary (infectious type). A number of counties in the western and coastal regions are endemic for leprosy, although sporadic cases have also been reported in non-endemic counties. Despite the apparent low number of cases reported annually in Kenya, 11% of the cases notified in 2019 were notified in patients below 15 years of age suggesting active transmission of leprosy in the community. Geographical variations are a striking feature of leprosy at every level. In Kenya, most new leprosy cases have been documented in Kwale, Kilifi, Kisumu, Siaya, Homabay and Busia counties.

1.1.3 Lung Health

The lung diseases asthma and chronic obstructive pulmonary disease (COPD) are very common. According to WHO, around the world 300 million people have asthma and 200 million have COPD. Low- to middle-income countries (LMICs) such as Kenya shoulder the burden of asthma and COPD. These diseases interfere with the lives of people, they stop people working and cost them money. The diseases also hold back countries from developing. The Ministry of Health through the division of National TB and Leprosy program has highlighted asthma and COPD as national priorities.

1.2 Strategic Focus

The National Tuberculosis, Leprosy and Lung Program (NLTD-P) strategic focus is to reduce the burden of lung disease and render Kenya free of TB and leprosy by finding the missing people with TB / Leprosy and providing timely and quality diagnosis, treatment and prevention to all high-risk populations. The NTLD-P is mandated to develop policies, build capacity and provide technical assistance to the devolved county system in Kenya. The program implements interventions within the framework of the National Strategic Plan for Tuberculosis, 2019-2023.

1.3 Diagnosis and Case Finding

The program is strengthening the surveillance system to ensure early testing and diagnosis through adoption of a new integrated diagnostic algorithm that incorporates chest x-ray for screening for TB, expansion of WHO recommended molecular GeneXpert and Line Probe Assays tests, as well as TB LAM and QuantiFERON Gamma. Additionally, facility based active case finding through systematic screening of all patients presenting to the health facilities, regardless of the presenting complaints, has been prioritized and is being implemented nationally to identify people with TB. Other case finding strategies include targeted community outreaches, contact tracing and screening and implementation of strategic innovative initiatives.

The patient pathway analysis conducted in 2017 demonstrated that 42% of the population preferred to seek initial care at the private facilities (15%, informal; 27% formal). Therefore, robust engagement with the private sector in TB prevention, care and control has been prioritized to ensure all private sector players have been engaged in the fight against the epidemic. This has realized a contribution of 15% to the total cases notified in 2019.

1.4 Integrated Care Provision

Further, integration of TB services at service delivery points in other program areas has also been instrumental in providing holistic TB prevention, care and control services. TB/HIV collaborative interventions are being implemented with intensified TB screening, HIV Testing among TB patients, prompt ART initiation among TB/HIV co-infected patients and TB preventive therapy among others. In 2019, the HIV testing rates of TB patients was 98% with a co-infection rate of 26% and ART uptake of 96%. The treatment success rate for the 2018 cohort was 84% against a target of 90%. Other integration areas include; TB and diabetes, reproductive, maternal and neonatal and child health (RMNCH) where screening and diagnosis for TB is being implemented.

1.5 Nutrition Status Assessment

Nutritional status is an important determinant of resistance to infection. Malnutrition increases the risk of developing TB and the vice versa. This predisposes the population to a higher risk of unfavorable outcome. In 2017, the NTLD-P conducted a TB Catastrophic Cost survey that found between 27.1% and 53.7%of TB affected households experienced food insecurity. Nutritional status assessment, intervention and monitoring is a crucial component of TB care and management. In 2019, 45% of the diagnosed drug susceptible and 54% of drug resistant TB were undernourished at the time of diagnosis.

1.6 Advocacy & Communication

The current advocacy and communication strategies identify the need to create an enabling environment for prevention of 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.

1.7 Recording & Reporting

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. 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.

1.8 Scope of the guidelines

The objective of these consolidated guidelines is to provide a public health approach and clinical guidance to the management of TB, leprosy and lung diseases. It aims at providing guidance and building capacity among health care workers (HCWs) on the provision of quality and universally acceptable services in diagnosis, treatment, prevention and rehabilitation of patients with these conditions. Additionally, it aims at providing guidance on linking 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 create demand for quality services. Towards this, it also calls for enhanced collaboration and coordination between the health care workers, communities, state and non-state actors, in order to realize universal coverage and comprehensive care in TB, leprosy & lung health services.

These guidelines are organized into the following sections: Case Finding strategies for TB,

TB in adults, TB in children, Laboratory diagnosis of TB, TB in Special conditions, Nutrition in TB, Drug Resistance TB, **Non-tuberculous Mycobacteria**, IPC, **LTBI,** Differentiated care of TB, Lung Health, Leprosy, Pharmacovigilance, ADSM, Commodity Management, Patient support, Human rights and Social protection, Communication and Advocacy, Community engagement, M&E

1.9 Target audience

The guidelines are targeted to all HCWs of various cadres who manage TB, Leprosy and Lung disease. They will also be used as part of the curriculum 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 the patients are catered for. 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.

APPROACHES TO FINDING PEOPLE WITH TUBERCULOSIS

2

2.1. Introduction

TB program is mandated to ensure provision of quality care for TB patients and enhance preventive strategies in the country. Of utmost priority is to mop out cases from the community to minimize the likelihood of continuous transmission in the population. Finding people with TB requires synergistic efforts from key stakeholders and can either be passive or active.

2.1.1 Passive case-finding

Requires that affected individuals are aware of their symptoms, have access to health facilities, and are evaluated by health workers or volunteers who recognize the symptoms of TB and who have access to a reliable laboratory.

2.1.1 Active TB Case Finding

Is the systematic identification of presumptive TB cases from a predetermined target group/population by doing symptomatic screening, detailed history taking, physical examinations and further laboratory and/or radiological investigations to diagnose TB.

2.1.3 Presumptive TB case

- This refers to a patient who presents with symptoms and/or signs suggestive of TB (previously known as a TB suspect).

Integration of ACF indicators in mainstream MOH tools

- Screening for TB (Under 5 and over 5) MOH 204A and MOH 204B
- Reporting on MOH 711

Strengthening contact management process

- Line listing contacts of pulmonary bacteriologically confirmed cases and invitation for TB screening
- Yield of diagnosed TB cases from contacts and under 5 initiated on TPT

Guidance on conducting facility outreaches.

- The determination of a true presumptive TB case should only be made by a clinician after detailed history taking and clinical examination to rule out other causes of respiratory illness.

2.2. Setting

TB case finding can be conducted at the health facilities and at the community level. These include:

1. Public and private health facilities including pharmacies, laboratories and individual clinics
2. Community
    a. Congregate settings e.g. prisons, schools, barracks, drug dens, refugee camps, places of worship and medical camps
    b. Workplaces

Approaches to TB case finding

Facility Based Active Case Finding (FB-ACF) involves screening for TB among all persons visiting a health facility at all service delivery points regardless of the presenting signs and symptoms.

Contact management involves systematic investigation of people who are in close contact with patients with infectious TB disease (index cases) and also reverse contact tracing for children under 5 years. After investigation, contacts found to have TB disease should be treated for TB according the National TB Treatment guidelines. Contacts without TB disease should be assessed for eligibility to TB Preventive Therapy *(Refer to chapter 11 on LTBI).*

Community outreach interventions including:

- Targeting congregate settings e.g., prisons, schools, drug dens, barracks, refugee camps, places of worship; workplaces, informal settlements, targeting the elderly among others.
- Other innovative approaches such as self-screening with linkage to health facilities

2.3. Facility Based Active Case Finding (FB-ACF)

2.3.1. Advocacy

Ownership by the management team is the cornerstone for successful execution of FB-ACF at a health facility. Hospital managers should spearhead FB-ACF by ensuring that;

- All the frontline Health Care Workers have undergone sensitization on FB-ACF (this should be done in liaison with the TB coordinators)
- Appointment of an ACF focal person; he/she should be a clinician working at the Outpatient Department (OPD)

- In liaison with the ACF focal person, each service delivery point (SDP) should calculate its targets based on their workload
- During facility monthly meetings, ACF should be discussed and each SDP presents their progress against targets, highlight the best practices and identifies key challenges/gaps/areas of improvement.
- Continuous quality improvement should be undertaken.

2.3.2. Patient Flow

TB screening should be administered to all patients presenting to the health facility regardless of presenting signs and symptoms. Proper understanding of the patient flow which is unique to each health facility provides a head start in ACF implementation. Back and forth of patients through the same departments should be avoided by ensuring that the patient is attended to holistically to reduce time taken at the health facility.

2.3.3. TB screening and Care Cascade

All patients should undergo the following;

1. Vital signs should be taken (fever as a key sign will be elicited at this point)
2. The triage personnel conducts TB symptomatic screening, the cardinal signs and symptoms of TB are:
    - Cough of any duration
    - Unintended weight loss
    - Drenching night sweats
    - Hotness of body
    - Chest Pain
    - BMI less than 18.5 of z-score ≤ -2

    For children, in addition to the above, the following should be considered;

    - History of frequent respiratory tract infections
    - Failure to Thrive
    - Reduced Playfulness
    - Lethargy and irritability
    - History of contact with a known TB case
3. All coughers should be fast tracked for assessment by a clinician.
4. The clinician performs detailed history taking and physical examination to determine the true presumptive TB cases to be sent for investigation for TB. Presumptive TB cases should be documented in the presumptive TB register and a sputum request form generated *(all fields should be properly filled for prompt relay of results).*

5. Presumptive TB cases should be sent to the laboratory/designated area for collection of samples after which the patient is advised on how to collect their results, then exited through normal facility procedures. In some facilities, clinicians can be sensitized on procedure for sample collection and a designated cough area identified, this will minimize on workload sent to the laboratory
6. Patients who are confirmed TB positive from the laboratory should be traced (phone tracing and where necessary home tracing), initiated on treatment and followed up. Those who receive a negative laboratory result should be followed up closely, should symptoms persist; further investigations can to be done to help confer a clinical diagnosis.

In the current TB diagnostic algorithm (Annex 2 & 3), chest X-ray can be used as a diagnostic tool for children. In settings where chest X-ray is readily available, it can be used as a screening tool and only those who are suggestive of TB should be referred for sample collection.

2.3.4. Linkage

Proper linkage at every step of patient's care is important to minimize leakages in the ACF cascade. Depending on the facility policy and human resources available, CHWs/CHVs/peer educators should link presumptive TB cases from the clinician to the laboratory and further to the chest clinic for those initiating TB treatment. Linkage also entails active phone and home tracing for those who with positive TB results to initiate treatment.

2.3.5. Recording and Reporting

Timely documentation is a key tentacle in the implementation of FB-ACF and as such the following recording and reporting tools are required:

- ACF screening tool - this outlines the cardinal signs and symptoms for TB and is used for symptomatic screening for TB
- OPD Register (MOH 204A & B) contains a column where the status of TB screening should be documented; this column provides information for all patients screened for TB at the health facility.
- Presumptive TB register - this is a register containing demographic and clinical information for identified presumptive TB cases; should be filled at the clinician desk
- Sputum Request Form - Upon successful identification of a presumptive TB case, the sputum request form should be duly filled by the clinician. The request form should be updated with details of the referring clinician to ensure seamless relay of results.

- TB laboratory register – Upon receipt of the TB lab request form, the laboratory officer should confirm the details and register the patients in the laboratory register. The referring department/peripheral health facility should be documented. The presumptive TB case is then provided with a falcon tube and instructed on how to collect a quality sample.
- ACF Departmental Summary Tool - this is the monthly summary of the ACF workload per Service Delivery Point, it provides a total of the number of patients offered TB screening and their movement across the entire care cascade. It should be filled at the end of the month by the departmental in-charge and obtains information from the OPD register, tally sheets, presumptive TB register, laboratory register and TB treatment register.
- ACF Facility Summary Tool - this is the monthly summary of the ACF workload at the facility, it documents the number of patients offered TB screening and their movement across the entire care cascade. It collates information from the ACF departmental summary tool and should be filled at the end of the month by the records department at the facility.
- MOH 711 - Select indicators from the ACF facility summary tool should be populated in MOH 711
- KHIS – Select indicators populated in MOH 711 should be uploaded into KHIS

The following should take place for successful implementation of ACF

- Orientation of health facility management team and health facility staff on quality improvement in TB case detection
- Formation of a TB coordinating team by the health facility management. (This can be integrated with other teams e.g. HIV coordinating team)
- Appointment of a health facility ACF TB focal person who should monitor ACF implementation per SDP and intervene promptly in case of any hitches
- Inclusion of TB case detection as a permanent agenda in the health facility clinical meetings by the health facility management
- TB coordinating team & ACF focal person to support each SDP to calculate their TB case detection targets based on their workload
- As a routine activity that should be entrenched in the health facility procedures; daily health education sessions with TB as an agenda, should be conducted to patients to create awareness
- Use of presumptive TB registers in all service delivery points in the health facility. A separate presumptive TB register should be kept for outreaches. All clients who screen positive for TB symptoms and subsequently undergo detailed assessment by a clinician and are determined to be true presumptive TB cases, should be recorded in the presumptive TB register.
- Introduction of Pediatric TB screening tool & presumptive register in various children-specific service delivery points including NMCH clinics, Nutrition clinic, Pediatric OPD clinic and all Pediatric wards. Accelerated TB case detection among children who are a high risk cohort for severe TB.
- All SDPs/Units or clinics should report on TB case finding indicators monthly – performance on FB-ACF, contact investigation and community outreach interventions.

- Health facilities should evaluate FB-ACF performance every month and take measures to resolve any pending challenges. This activity should be led by the Facility in charge, ACF committee and ACF focal person. Discussions should be documented and form a basis for continuous quality improvement.
- Supportive supervision and mentorship to unit/clinic staff should be conducted regularly.

2.3.6. Target Setting

Targets provide a premise upon which performance can be assessed and lays a basis for continuous quality improvement. Targets vary depending on the catchment population and facility workload. Each health facility and subsequently service delivery point, should set their targets monthly in liaison with the ACF Focal person.

Based on their workload, the following guiding principles should be used;

- 15-30% of all patients seen at the health facility have respiratory infection
- 60-80% of the patients presenting with respiratory infections are presumptive TB cases and should be investigated to rule out TB
- At least 10% of presumptive TB patients should be TB cases (Bacteriologically confirmed and clinically diagnosed)
- 10-15% of TB cases should be children under 15 years of age.

2.3.7. Monitoring

Monitoring is both internal and external and should be done continuously to flag out underperformance early and plan for corrective action. Internally, during the facility monthly meetings, performance/progress against targets per SDP should be reviewed, best practices and challenges highlighted, to encourage cross-learning.

Periodic county and sub county supervisions should incorporate key indicators on FB-ACF to assess the progress on TB case finding. This should provide an opportunity for continuous mentorship and sensitization.

2.3.8. Continuous Quality Improvement

In FB-ACF, each facility should strive to get better by learning through the process. This can be attained by ensuring efficiency in screening, enhancing a high index of suspicion among Health Care Workers and closing leaks in the care cascade hence minimizing on numbers needed to screen to get a confirmed TB case.

Continuous quality improvement should be undertaken as per the steps below;

- Establish a Quality Improvement team
- Define the problem by clearly establishing the actual versus desired performance of a key indicator

- Agree upon opportunity for improvement and determine methodology to be used
- Monitor and evaluate the entire process
- Repeat this process until desired performance/standards are attained

Note:

- Target setting is based on the workload of the facility and may vary across the year.
- Proportion of clients with respiratory conditions among the OPD attendance vary from one location to another, based on morbidity pattern in the geographical area.
- The clinician assessment (history taking and physical examination) is key in determining the quality of care to the patients as well as establishing the true presumptive TB cases to be investigated.
- Monthly review of data through each step in the patient care cascade is key in determining leakages. The review should involve health care workers; linkage assistants, records officers, clinicians, departmental heads, ACF TB focal person, TB/HIV coordinator, laboratory technician, pharmacist, CHEW and facility in-charge. Where applicable, the Sub County team should be in attendance (Sub County TB and Leprosy Coordinator/Sub County clinical officer/Sub County Public Health Officer/Sub County Medical Laboratory Coordinator).

2.3.9. Roles and responsibilities

A. Role of front-line health care workers

a) Triaging personnel (HCWs/CHVs/cough monitors/records person)

- Initial symptomatic TB screening and referral to the clinician.
- Link clients to the clinician, laboratory and treatment
- Follow up confirmed TB patients who fail to return for treatment initiation (by CHVs).
- Contact tracing and referral of people with signs and symptoms of TB from community

b) Clinicians at all Service Delivery Points

- Clinical evaluation through conducting detailed history taking and physical examination to determine true presumptive TB cases. Provide health education to the presumptive TB cases to understand why investigations are required to rule out TB.
- Document on the presumptive TB register, complete the TB laboratory request form and send presumptive TB cases for GeneXpert/ smear microscopy (CXR as appropriate)
- Populate in the presumptive TB register the laboratory results once received.

- Interpret the laboratory results and manage the patients accordingly.
- If TB is diagnosed whether bacteriologically or clinically, prescribe and refer patients to TB clinic for treatment initiation, contact management and follow up.
- Review the TB screening data across the care cascade and present in the ACF monthly meetings.
- Participate in ACF monthly review meetings.

c) Laboratory personnel:

- Receive the patient at the laboratory and explain the process of quality sputum collection and turnaround time for results
- Carry out laboratory tests and relay results back to the referring clinicians. Where applicable, use the linkage assistant to relay the results back to the clinician.
- Follow up all confirmed TB patients (from the laboratory register) to return for treatment initiation.
- Review the monthly TB laboratory data and present during the monthly ACF data review meetings.
- Participate in ACF monthly review meetings.

d) Roles of Clinicians in the TB clinic

- Evaluate all patients referred to TB clinic for treatment initiation (history & physical examination) and provide health education to the patient. Capture the demographic and clinical details in the patient record cards and attach the laboratory results where applicable.
- Document the patient in the TB register and initiate treatment.

  Ensure the appointment card in populated and issued to the patient.
- Line list all contacts of pulmonary bacteriologically confirmed TB patients and children <5 with TB in the TPT/Contact management register. The contacts should then be invited to the facility for assessment and further evaluation for TB.
- Inform CHVs of any contacts who have not been screened for follow up in the community
- Ensure the patients are notified through the SCTLC
- Analyze the data and present during monthly ACF meetings at the health facility.

e) Roles of HRIOs

- Compile the data along the cascade of care for patients who undergo TB screening at the health facility.
- Reporting TB screening and case finding data on national reporting databases (DHIS)
- Analyze the ACF care cascade data from the departments starting from the workload and respiratory conditions reported within the month – OPD, In-patients, Maternity, MCH/Child Wellness clinics, special clinics etc.

- Participate in monthly ACF meetings and present the progress against facility target.

B. Role of county and hospital managers

a) Hospital Management Team (HMT)

- Provide leadership at facility level on ACF target setting, improving diagnosis, IPC, TB treatment and follow up
- Provide leadership on the use of data for planning and decision making in their facilities

b) County & Sub-County Health Management Teams (CHMT/ SCHMT)

- Provide leadership of TB control services in the County/ Sub-County (Champion ACF agenda and target setting)
- Provide leadership on ACF data use for planning and decision making in their Counties/ Sub-Counties

c) County TB and Leprosy coordinator (CTLC)

- Provide oversight of TB programming in the county
- Build capacity of SCTLCs and HCWs on TB through micro-teachings, on-job mentorship, facility CMEs and by availing job aids, SOPs and guidelines
- Conduct support supervision

d) Sub-county TB and Leprosy coordinator (SCTLC)

- Avail TB recording and reporting tools
- Provide oversight of TB programming in the sub-county
- Build capacity of HCW on TB through micro-teachings, on-job mentorship, facility CMEs, and by availing job aids, SOPs and guidelines
- Conduct support supervision to healthcare workers
- Ensure timely notification of TB patients in TIBU.
- Participate in the ACF monthly meetings

e) County Medical and Laboratory Technologist (CMLT)

- Provide oversight on TB laboratory procedures in the county
- Ensure reporting on TB laboratory consumables in the county
- Build capacity of SCMLTs and HCWs on laboratory procedures for TB through micro-teachings, on-job mentorship, facility CMEs and by availing job aids, SOPs and guidelines
- Conduct support supervision

f) Sub-county Medical and Laboratory Technologist (SCMLT)

- Provide oversight on TB laboratory procedures in the sub county
- Ensure reporting on TB laboratory consumables in the sub county
- Build capacity of HCWs on laboratory procedures for TB through micro-teachings, on-job mentorship, facility CMEs and by availing job aids, SOPs and guidelines
- Conduct support supervision

C. Role of community members and other players

Community health workers/ volunteers and other community players e.g. Civil Society Organizations

- Sensitize communities on TB
- Screen community members for TB including contacts who are not able to go to the health facilities
- Refer and link community members who require further evaluation to health facilities
- Liaise with health facilities to trace and return TB treatment interrupters back to treatment

2.4 Contact Management

During enrolment to TB treatment, health care workers should line list contacts of all pulmonary bacteriologically confirmed TB patients (index case) and children under 5 with TB (reverse contact tracing). The contacts can be drawn from the household, social and work places. All listed contacts should be screened for TB at the health facility or in the community i.e. households, schools and workplaces. Contacts who are presumptive TB cases should be managed in line with the TB diagnostic algorithm (Annex 2 & 3). Index cases should be advised to bring their contacts to the health facility for TB screening.

2.4.1. Definitions for Contact Investigation

a) Index case/ Index patient

The initially identified case of new or recurrent TB in a person of any age in a specific household or other comparable setting in which others may have been exposed.

Priority should be given to index patients who have any of the following characteristics:

- Has bacteriologically confirmed pulmonary TB
- Is a child <5 years with TB (to find the source of infection)
- DRTB cases (proven or suspected)

Note: *If resources are available, contact investigation may be conducted for index patients of lower priority such as those with clinically diagnosed pulmonary TB*

b) Contact

Any person who has been exposed to an index case. There are two types of contacts:

i) Household contact

A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode

Note: *Definitions of 'household' vary considerably and must be adapted to the local context. Within households, there is a gradation of exposure, ranging from sharing the same bed as the index case to living in the same compound but not in the same enclosed space.*

ii) Close contact

A person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.

2.4.2. Contact Investigation

A systematic process intended to identify previously undiagnosed cases of TB among the contacts of an index case.

Contact investigation consists of two components:

2.4.2.1. Contact Identification and Prioritization

A systematic process to identify contacts with or at increased risk for development of TB. This includes:

- An interview with the index case to obtain the names and ages of contacts
- Line listing of all contacts in the contact management register
- An assessment of contacts' risk for having or developing TB, based on the presence of TB signs and symptoms, to determine those for whom clinical evaluation is indicated.

2.4.2.2. Clinical Evaluation

A systematic process for the diagnosis or exclusion of active TB among contacts who have signs and symptoms of TB. Clinical evaluation should be done in accordance with the TB diagnostic algorithm (Annex 2 & 3).

Priority should be given to the following contacts:

- People of all ages with signs and symptoms suggestive of TB
- Children <5 years of age
- People with known or suspected immunocompromising conditions (especially PLHIV)
- Contacts of index cases with DRTB (proven or suspected)

2.4.3. Reverse Contact Tracing

A source case investigation (also known as a 'reverse contact investigation') is a type of contact investigation done to identify the source case of someone recently diagnosed with active TB disease. Source case investigations are recommended when children less than 5 years old are diagnosed with active TB disease and in the event of pleural TB (primary TB) in a younger person.

Source case investigations focus on identifying and screening those most likely to have TB disease among the people that spent the most time with the index case.

For index cases that are children, source cases are most likely to be found among adolescents or adults from:

- Within the household (persons living in the home, frequent visitors, babysitters)
- School
- Daycare
- Carpools or school buses
- Playgroups
- Places of recent travel

2.4.4. TB Screening and Care Cascade

Screening of contacts should be addressed based on whether the contact was invited (contact invitation) or traced (contact tracing).

2.4.4.1. Contact Invitation

Contact invitation is when the index patients brings his/her contacts to the hospital for TB screening. All invited contacts should undergo the following;

1. Vital signs should be taken (fever as a key sign will be elicited at this point)
2. TB symptomatic screening, the cardinal signs and symptoms of TB are:
    - Cough of any duration
    - Unintended weight loss
    - Drenching night sweats
    - Hotness of body
    - Chest Pain
    - BMI less than 18.5 of z-score ≤ -2

    For children, in addition to the above, the following should be considered;
    - History of frequent respiratory tract infections
    - Failure to Thrive
    - Reduced Playfulness

- Lethargy and irritability
- History of contact with a known TB case

3. The clinician performs detailed history taking and physical examination to determine true presumptive TB cases who are then documented in the presumptive TB register and generates a sputum request form.
4. Presumptive TB cases should be sent to the laboratory/designated area for collection of samples after which the patient is advised on how to collect their results, then exited through normal facility procedures. In some facilities, clinicians can be sensitized on procedure for sample collection and a designated cough area identified, this will minimize on workload sent to the laboratory
5. Patients who are confirmed TB positive from the laboratory should be traced and initiated on treatment; while those who receive negative laboratory confirmation should be followed up closely and in the event that symptoms persist, further investigations need to be done to confer a clinical diagnosis.
6. Contacts who screen negative for all the symptoms and are eligible for preventive therapy, should be initiated on TPT ***(refer to Chapter 11 on LTBI)***, otherwise they are discharged in line with hospital policies and advised to come for follow up TB screening every six months.

2.4.4.2. Contact Tracing

Contact tracing is initiated when an index case fails to bring his/her contacts to the hospital for TB screening. The CHV/CHW is then given a list of all the listed contacts to trace from the community.

All traced contacts should undergo the following;

1. Vital signs should be taken (fever as a key sign will be elicited at this point)
2. TB symptomatic screening, the cardinal signs and symptoms of TB are:
    - Cough of any duration
    - Unintended weight loss
    - Drenching night sweats
    - Hotness of body
    - Chest Pain
    - BMI less than 18.5 of z-score ≤ -2

    For children, in addition to the above, the following should be considered;
    - History of frequent respiratory tract infections
    - Failure to Thrive
    - Reduced Playfulness
    - Lethargy and irritability
    - History of contact with a known TB case

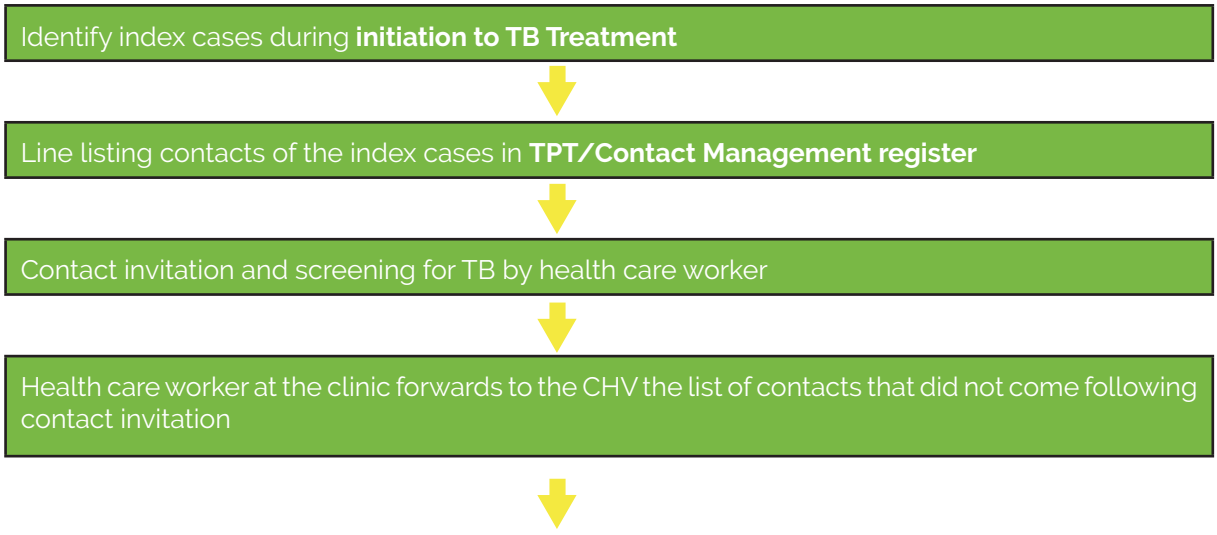
3. The clinician performs detailed history taking and physical examination to determine true presumptive TB cases who are then documented in the presumptive TB register and generates a sputum request form.
4. Presumptive TB cases should be sent to the laboratory/designated area for collection of samples after which the patient is advised on how to collect their results, then exited through normal facility procedures. In some facilities, clinicians can be sensitized on procedure for sample collection and a designated cough area identified, this will minimize on workload sent to the laboratory
5. Patients who are confirmed TB positive from the laboratory should be traced and initiated on treatment; while those who receive negative laboratory confirmation should be followed up closely and in the event that symptoms persist, further investigations need to be done to confer a clinical diagnosis.
6. Contacts who screen negative for all the symptoms and are eligible for preventive therapy, should be initiated on TPT ***(refer to Chapter 11 on LTBI),*** otherwise they are discharged in line with hospital policies and advised to come for follow up TB screening every six months.

2.4.5. Recording and Reporting

Adequate contact management helps to curtail the TB transmission process and as such monitoring the yield of contact investigation can only be attained through proper documentation in the following tools:

- TPT/Contact management register - during enrolment of an index case, the HCW should line list all their household and close contacts (household, work, social). Further, these contacts should be invited for TB screening and their screening status documented in the same register.
- Contact tracing log - for those patients who are traced in the community; both phone and home tracing should be documented

2.4.5.1 Contact Investigation Data Flow



CHVs use the **TB screening/community contact tracing form** to screen contacts of the index cases and refer those contacts with TB symptoms to the health facility. All contacts <5, PLHIV and contacts of MDR and XDR TB patients should be referred using the **Community Referral form MOH 100.**

CHV returns the forms to the health facility. Each form represents an index patient and their contacts

The health care worker verifies the forms, updates the contact management/TPT register and begins investigations for those who are presumptive TB cases as guided in the TB diagnostic algorithm (Annex 1 & 2).

**All household and close contacts should be counseled and tested for HIV*

2.4.5.2. Monitoring

Monitoring should be both internal and external and should be done continuously in order to detect underperformance early and plan for corrective action. Internally, during the monthly meetings, performance/progress against targets should be reviewed. Periodic county and sub county supervisions should incorporate key indicators on contact management to assess the progress on case finding and TPT uptake. This should provide an opportunity for continuous mentorship and sensitization.

2.5. Community Outreaches

2.5.1. Advocacy and Social Mobilization

CHWs/CHVs/peer educators, opinion leaders, local administration, religious leaders and local policy/political leaders should be sensitized on their role in TB control efforts in the community. Community outreach interventions should be guided by disease burden, health seeking behaviour and/or linkage to availability of TB services.

A multi-sectoral approach through engagement of key stakeholders to reach their populations e.g. education (schools, colleges,) transport (matatu industry, association of long distance truck drivers), should be used. These interventions should include appropriate linkage to health facilities for further management.

2.5.2. Client Flow

- Initial screening should be done using TB signs and symptoms
    - Cough of any duration
    - Unintended weight loss
    - Drenching night sweats
    - Hotness of body
    - Chest Pain
    - BMI less than 18.5 of z-score ≤ -2

- Clients who screen symptom positive should be offered chest X-Ray. It is only those clients with radiographs interpreted as *"Abnormal Suggestive of TB"* who should provide samples for laboratory diagnosis.
- After TB screening and determination of a true presumptive TB case, the client should produce a sputum sample for TB screening and other necessary tests.
- Those who are confirmed with TB should be linked to the nearest TB treatment site and/or CHV of their community unit.
- The outreach team should always comprise of clinicians who will determine the true presumptive TB cases and assess the need of initiating severely ill patients on TB treatment during an outreach activity, however, they should ensure adequate linkage mechanisms for follow up visits.
- Clients with negative laboratory results should be evaluated further, treated for the other lung diseases and closely monitored for possibility of a clinical diagnosis should the symptoms recur.

During targeted outreaches, chest X-ray should be used as a screening tool. It is only those with radiographs *"Abnormal Suggestive of TB"* who should be eligible to provide samples for laboratory diagnosis.

- Contacts of those who are confirmed with TB should also be screened.
- Contacts who are asymptomatic should be assessed for TPT eligibility. For those eligible; TPT should be initiated, the rest should be discharged according to the hospital policy and advised to come for follow up screening every six months.

Considerations for case finding among special populations

- **Health care workers:** Screen biannually using the TB screening questions. A contact management / TPT register should be introduced at all health facilities to capture data on health care workers screening (Name, department, cadre, screened for TB - yes/no, presumptive - yes/no). Further management should be documented in the presumptive register. This will also include students for practicals, interns and volunteers working in health institutions.
- **Residential institutions (Prisoners and prison staff, People residing in shelters and other congregate settings such as the military):** Screen at entry and every six months. Continuous surveillance should be conducted routinely in the prisons.
- **Detainees (in police cells) and remandees:** There is a need to ensure that detainees and remandees are screened and investigated as appropriate. Ensure comprehensive contact information is provided to support linkage with the health facilities for those who are presumptive.

- **Students in learning institutions:** The medical examination at entry requires a chest x-ray done. Ensure the chest x-ray is interpreted and reported. A GeneXpert test to be requested for any abnormal chest x-ray report. School clinics should liaise with nearby health facilities for reporting and linkage to diagnostic facilities.
- **Community:** Geographical areas with a high prevalence and subpopulations with poor access (poor populations, urban slums, remote areas, refugees, homeless)
- **Hospital outpatient and inpatient departments, and primary health-care centres:** People previously treated for TB, People with an untreated fibrotic lesion, People living with HIV and people attending HIV testing, People with diabetes mellitus, People with chronic respiratory disease and smokers, Undernourished People with gastrectomy or jejuno-ileal bypass, People with an alcohol or drug-use disorder, People with chronic renal failure, People on immunocompromising treatments, Elderly people, People in mental health clinics or institutions
- **Immigration and refugee services:** Immigrants from settings with a high prevalence of TB, People in refugee camps
- Workplaces: Miners or others who are exposed to silica, Other workplaces with a high prevalence of TB

2.5.3. Community Outreach Data Flow

Health care workers screen community members and fill the community TB screening form

↓

Health care workers list presumptive TB cases in a designated presumptive register for outreaches which should be kept at the TB clinic

↓

People presumed to have TB are linked to the health facility and managed according to the TB diagnostic algorithm (Annex 1 & 2)

↓

Discharge from the health facility should be through the CHVs/CHWs in their respective community units for adequate follow up

Quality Assurance

The following are steps to ensure quality in TB case finding

- Training of health care workers in TB, including in TB case finding
- Provision of guidelines, job aids and SOPs to healthcare workers
- Ensuring clinician review for all patients screened by non-clinicians and labelled as presumptive
- Use of and adherence to standard MOH tools for recording and reporting and diagnostic algorithm (Annex 1 & 2)

- Following up patients along the entire cascade of care to minimize leakages and ensure those with TB receive prompt treatment and the rest get appropriate care.
- Correct and complete documentation and timely reporting
- Regular data review
- Mentorship and supervision by facility, sub-county and county leadership teams

MANAGEMENT OF DRUG SUSCEPTIBLE TUBERCULOSIS (DSTB) IN ADULTS

3

3.1 Introduction

3.1.1 Definition

Tuberculosis (TB) is an airborne chronic infectious disease caused by *Mycobacterium tuberculosis*. It usually infects the lungs, but it can infect any part of the body such as the kidney, spine, and brain except the nails, hair and teeth. If not treated properly, TB disease can be fatal.

3.1.2 Aetiology

TB disease is caused by a pathogenic bacteria called *Mycobacterium tuberculosis* (M. tuberculosis) from the family Mycobacteriaceae. *M. tuberculosis* is one of the very closely related *M. tuberculosis complex* species which include *M. bovis*, *M. africanum*, *M. microti*, *M. caprae*, *M. pinnipedii*, *M. canetti* and *M. mungi*. 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 Non-tuberculous Mycobacteria (NTM) may cause a disease similar to typical TB infection with *M. tuberculosis*.

KEY HIGHLIGHTS:

1. **Chest x-ray has a role in TB screening and diagnosis**
2. **New diagnostic techniques have been introduced, including Gene Xpert Ultra and TB-LAM**
3. **Algorithm for TB diagnosis has been revised and includes TB screening and guidance on interpretation of results and follow up of persons with TB**
4. **Dosage of anti-TB medicines is weight based and now accommodates dosing for those > 70kg**
5. **In Kenya, DSTB is treated using four medicines in fixed dose combination formulation**

3.2 Classification of Tuberculosis

3.2.1 TB Case Definitions

The following are case definitions used to classify TB cases initially:

a) **A presumptive TB case:** one who presents with symptoms or signs suggestive of TB

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

c) **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 extra-pulmonary cases without laboratory confirmation. **Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.** All such cases should be notified regardless of whether TB treatment was started or not.

All bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to the following:

1. Anatomical site of disease
2. History of previous treatment
3. HIV status
4. Drug resistance

This classification is summarized in the table below:

Table 3.1: 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	Manage as a previously treated patient
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 (refer to DR TB chapter)	
Drug Susceptible TB	Any bacteriologically confirmed case of TB with no evidence of resistance to any of the first line anti-TB medicines
Drug Resistant TB	Any bacteriologically confirmed case of TB with confirmed resistance to any of the first line medicines. It also includes cases with confirmed resistance to second line anti-TB medicine.

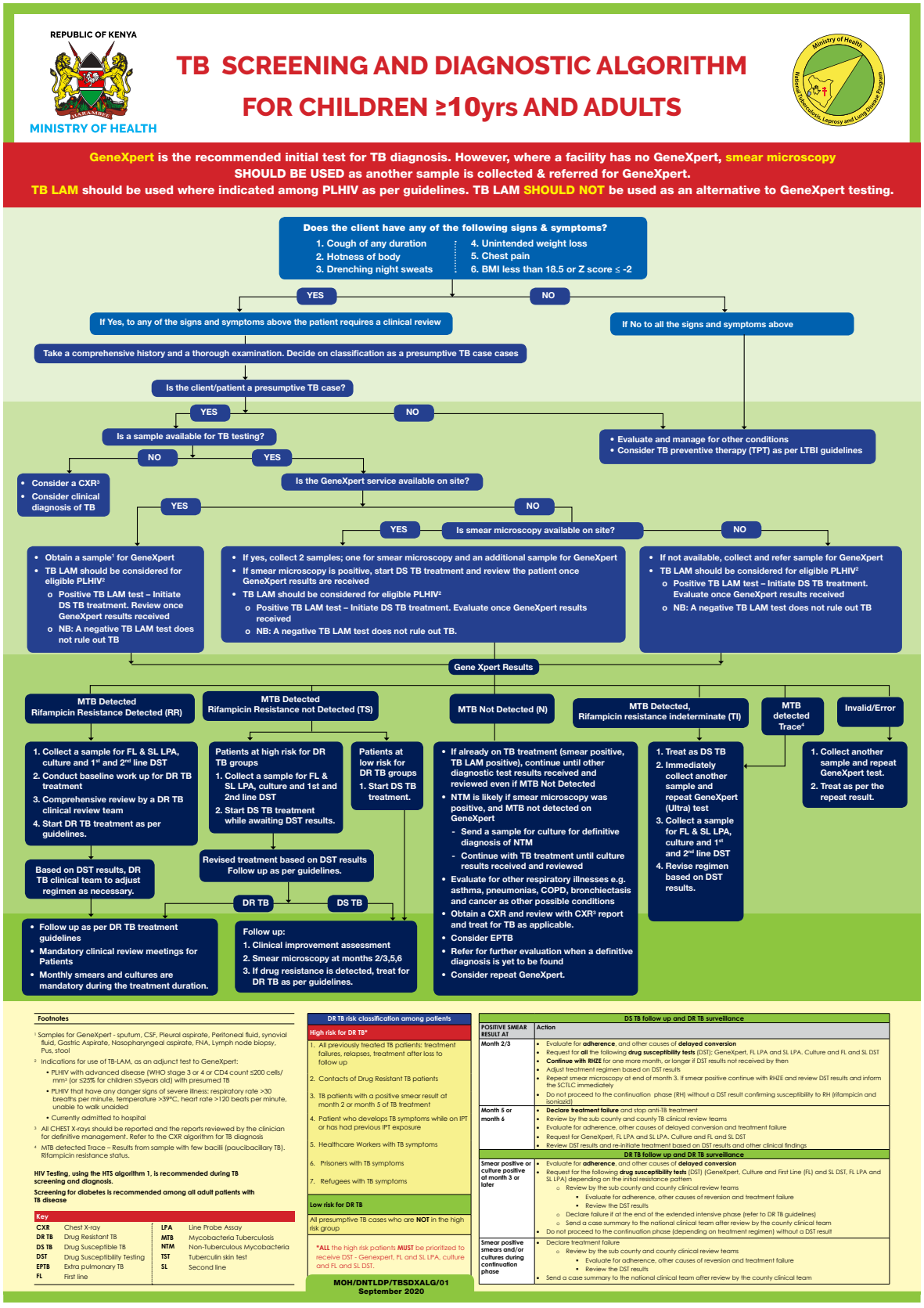
3.3 Diagnosis of Tuberculosis

Active TB case finding is key in diagnosis of TB in adults and adolescents. This involves screening all persons visiting health facilities using key screening questions which include presence of:

1. Cough (of any duration)
2. Hotn;ess of body/ body temperature > 37.5° C
3. Drenching night sweats
4. Unintended weight loss/ BMI less than 18.5
5. Chest pain

Persons who screen positive for any of the signs and symptoms listed above should undergo a thorough clinical evaluation before classification as a presumptive TB case. Presumptive TB cases should undergo diagnostic evaluation as per the TB screening and diagnostic algorithm for adults and adolescents >10years shown below:

Figure 3.1: TB Screening and Diagnostic Algorithm for Adults/ Children > 10years



To make a diagnosis of Tuberculosis disease, the following steps should be followed:

A) History Taking

TB diagnosis begins with taking a thorough medical history. TB should be ruled out in any person presenting with any of the signs and symptoms of TB, and history of contact with a TB patient. The aim of history taking is to rule out other differential diagnoses of TB disease which are shown below:

Table 3.2: Differential Diagnosis of Pulmonary Tuberculosis

Disease	Presentation	Distinguishing From PTB
Chronic Obstructive Pulmonary Disease (chronic bronchitis /emphysema)	Exertional dyspnea, chronic cough and sputum production	Lung function tests (spirometry), imaging
Heart failure	Exertional dyspnea, chronic cough, orthopnea, edema	Imaging (CXR, echocardiogram) shows cardiomegaly, ECG, laboratory tests
Bronchiectasis	Chronic cough, daily mucopurulent sputum production	Lung function tests (spirometry), CT scan imaging
Lung abscess	Fever, cough and sputum production	Culture results, imaging usually shows infiltrates with a cavity
Lymphoma	Rapidly growing mass with fever, night sweats and weight loss	CXR CT Histopathology
Lung cancer	Cough, hemoptysis, chest pain and dyspnea	Histopathology
Sarcoidosis	Chronic cough, dyspnea, chest pain	Histopathologic detection of noncaseating granulomas
Fungal pneumonia e.g. *Aspergillus*, *Histoplasma*	Fever, chest pain, shortness of breath, cough, and/or hemoptysis	Exposure history and culture results

B) Physical Examination

Physical signs of TB on respiratory examination may include tachypnea, bronchial breath sounds, dullness on percussion, reduced air entry, fever > 37.5^{0} C, wasting, haemoptysis and pallor.

If the patient does not have any of the signs/ symptoms above or is not found to be a presumptive TB case on further clinical review, evaluate the patient for TB preventive therapy (refer to Chapter 11: Latent TB infection management)

C) Investigations for Diagnosis of PTB

GeneXpert MTb/ Rif is the preferred first test of choice for TB diagnosis and detection of rifampicin resistance. All persons with Presumptive TB should undergo microbiologic testing to confirm the diagnosis. Key considerations in the choice of TB diagnostic test to be used include:

- When GeneXpert testing is available on site, a sputum sample should be collected and sent for GeneXpert testing.
- When only smear microscopy is available on site, 2 sputum samples should be collected, one for smear microscopy, and the other to be transported to the nearest GeneXpert testing laboratory. If smear microscopy is positive, the patients should be started on DS TB treatment and reviewed once GeneXpert results are received. **A negative smear microscopy result does not rule out TB**.
- If both GeneXpert and smear microscopy are not available on site, a sputum sample should be referred to the nearest GeneXpert testing laboratory.
- TB LAM should be considered for eligible PLHIV as per the diagnostic algorithm. If positive, initiate DS TB treatment and review once GeneXpert results are received. **A negative TB LAM result does not rule out TB**.
- All adult patients newly diagnosed with TB should undergo HIV testing as per the HTS algorithm and Diabetes testing as per the Kenya Diabetes guidelines.

Table 3.3: Tuberculosis Investigations

Investigation	Target	Purpose
1.GeneXpert and GeneXpert ultra	Preferred test of choice for all presumptive TB cases	For diagnosis of TB and detection RR TB
2.Smear microscopy (Fluorescent and Light microscopy)	All presumptive Pulmonary TB where GeneXpert is not available All DSTB patients for treatment follow up.	Detect TB disease. Monitoring of bacteriologically confirmed TB patients on treatment at months 2/3, 5 and 6
3. Chest X-ray	Preferred for all presumptive pulmonary and some extra pulmonary TB where accessible and affordable	A screening tool to identify those at high risk of TB disease. Supports TB diagnosis especially in children and when sputum for AFB/ GeneXpert is negative or not applicable
4. Histology	All presumptive EPTB	Tissue diagnosis in suspected EPTB e.g. TB adenitis
Other supportive tests		
Tuberculin skin test and IGRA	For detection of TB infection	Used in detection of latent TB infection

Lateral flow urine lipoarabinomannan assay (LF-LAM)	HIV infected patients with severe illness or advanced disease All hospitalized PLHA	For diagnosis of TB as an add-on test to GeneXpert/ GeneXpert ultra It is an add-on test to GeneXpert testing to increase diagnostic yield of TB testing in severely immunocompromised PLHA.
All attempts must be made to make a bacteriological diagnosis of PTB in adults.		

3.4 Baseline Work Up for Newly Diagnosed Tuberculosis

Adult patients newly diagnosed with TB should receive the following care once they are received at the TB clinic:

1. Detailed clinical evaluation including history of previous treatment and co-morbid conditions
2. Patient education, counselling (including adherence counselling, substance abuse counselling and mental health assessment)
3. Nutritional assessment, diagnosis and management
4. Where accessible, a baseline chest X-ray should be done for persons with pulmonary TB
5. Line listing of all contacts, contact invitation/ tracing and management.
6. Initiation of treatment and follow up during treatment

3.5 Role of Chest X-ray (CXR) in Tuberculosis Screening and Diagnosis

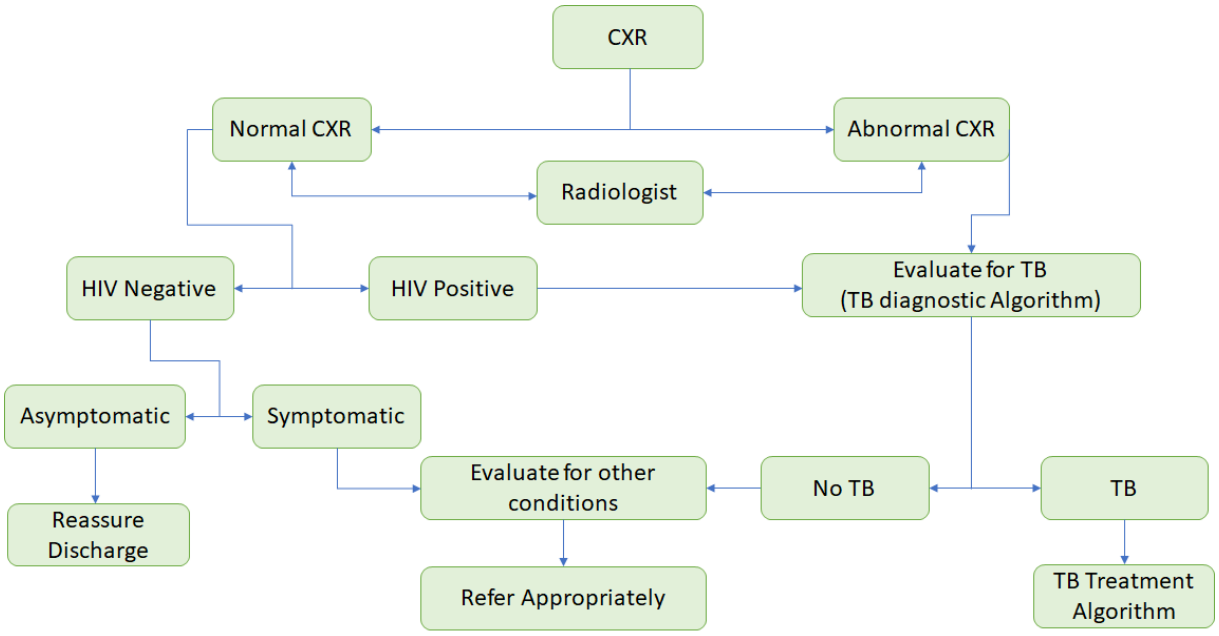
1. Screening tool for tuberculosis in those at risk (used to stratify for risk of TB and to assess for asymptomatic active disease) or during targeted outreaches to screen those eligible for testing.
2. As an aid in diagnosis of active Pulmonary TB and some EPTB (pleural, pericardial, nodal, spine).
3. Used to differentiate latent TB vs active TB based on the radiographic findings.
4. To characterize radiographic abnormalities so as to exclude other differential for appropriate referral and management.
5. Useful in the follow up treatment response based on clinical status (for patients who are not improving in the first month of treatment or patients who get worse after initially improving clinicaly.
6. Detection of complications of active TB disease and post TB sequelae.
7. Baseline CXR examination to support comparative evaluation during treatment and follow up of patients.

Where accessible, pulmonary TB patients should have a CXR at the beginning of treatment and at the end of treatment at 6 months

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

The algorithm below should be used in the diagnosis of TB.

Figure 3.2: Chest X-ray Algorithm for TB diagnosis



3.5.1 Recommended Radiographic Views and Utility

Standard Views	
View	**Indication**
Postero-anterior (PA)	Standard View for All adults
Antero-posterior (AP)	For patients unable to stand including the very sick, elderly and children
Additional Views (to be recommended by the radiologist)	
Lateral	As an aid to PA and AP view to evaluate the mediastinum, hilar regions, the posterior lung and spine
Lordotic	To evaluate subtle changes in the lung to provide better visualization.

Apical	To evaluate subtle changes in the Apical segments of the upper lobes to provide better visualization
Lateral decubitus	To rule out small pleural fluid in the presence of blunting of the costophrenic angles

3.5.2 Image Reporting

Chest X-rays should be reviewed by a clinician for definitive management and referral as appropriate. Abnormal chest x-rays should be reported by a radiologist for confirmation of the diagnosis.

3.5.3 Radiographic Findings in Pulmonary Tuberculosis

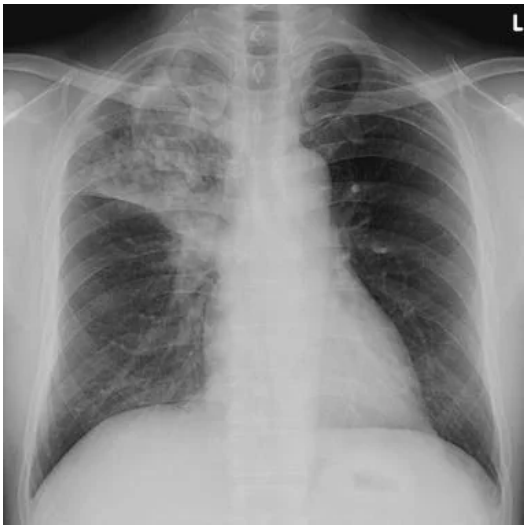
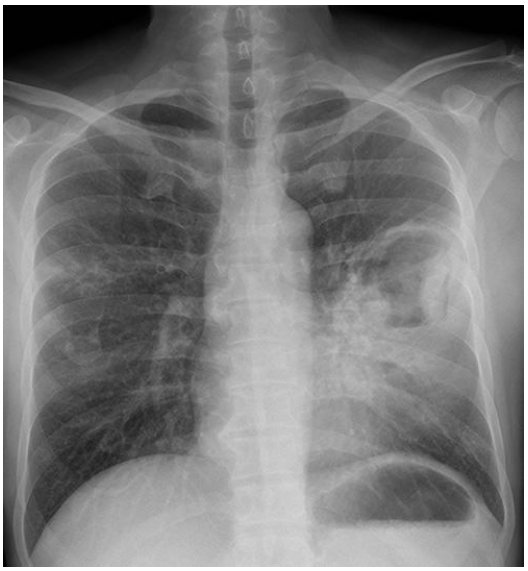
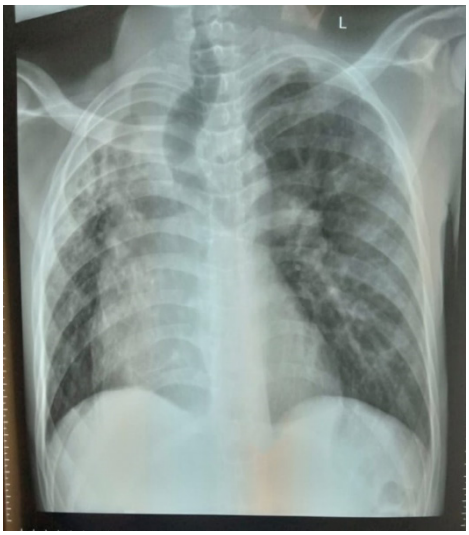
Tuberculosis disease exhibits a varied range of radiographic patterns in the lung depending on the patient immunological status, exposure whether recent or past and duration of infection. It can be primary or post primary, typical or atypical.

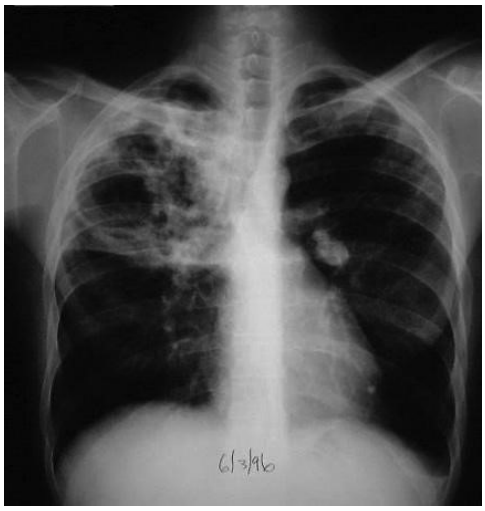
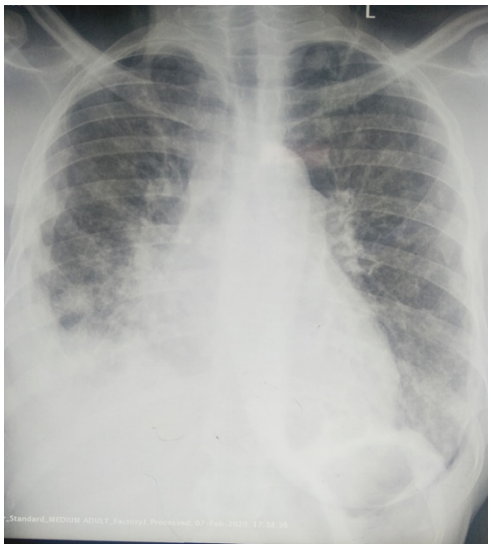
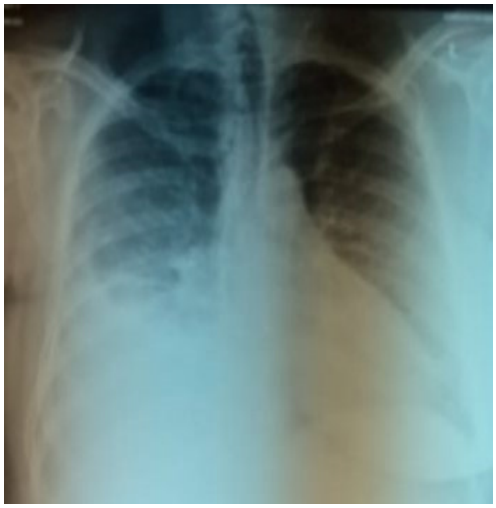
Type of TB	Possible radiographic findings
Primary TB	Lymphadenopathy, consolidation, pleural effusion Milliary nodules
Post primary TB	Consolidation and/or focal infiltration mainly involving the apical or posterior segments of the upper lobes and superior segments of the lower lobes, cavitation, nodules or fibrosis

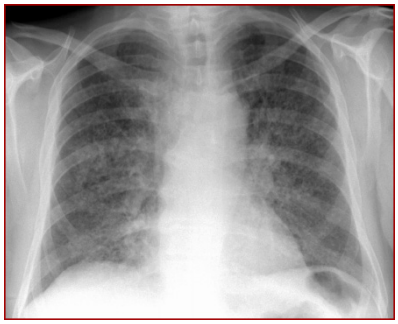
In HIV infected persons, with intact immunity, the radiographic picture is often typical. In advanced HIV with severe immunosuppression, the radiographic picture is more often atypical with lower or mid-zone shadows and the presence of hilar or mediastinal lymph node enlargement or pleural effusions being relatively common.

The radiographic findings could also be normal especially in advanced HIV immunosuppression. Table 3.4 outlines some common chest x-ray findings suggestive of pulmonary TB.

Table 3.4: Examples of Pulmonary Tuberculosis Radiographic Findings (Figures sourced from *Chest X-rays made easy: Christopher Clarke; 2020***)**

Radiograph	
	**Findings** Right apical consolidation, cavitation and fibrotic changes with elevation of the minor fissure.
	Left lingula segment consolidation and cavitation. Intracavitary aspergillosis is also a possibility. Right mid zone parenchymal infiltrates and nodules are also demonstrated
	Right sided fibrosis with marked volume loss/ retraction of the upper lobe. Right apical thick irregular pleural capping. Left upper lobe nodular lesions and a cavitary lesion.

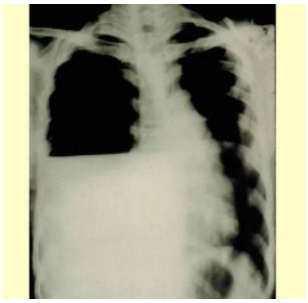
	Right upper lobe consolidation, cavitary lesions and fibrosis.
	Diffuse parenchymal infiltrates and nodular lesions. Right pleural effusion. Cardiomegaly
	Right pleural effusion. Parenchymal infiltrates. Cardiac patient.

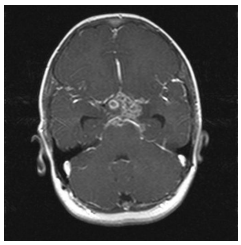
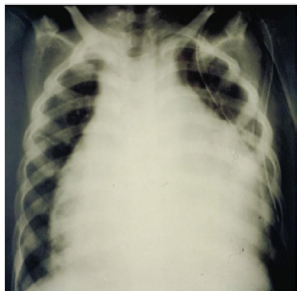
Miliary TB 	• Miliary TB with Miliary lesions on chest X-ray.

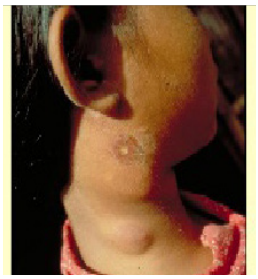
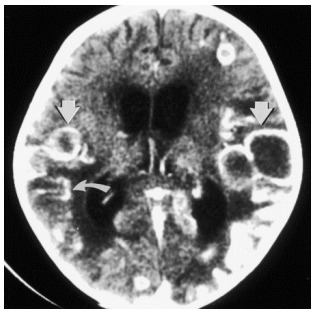
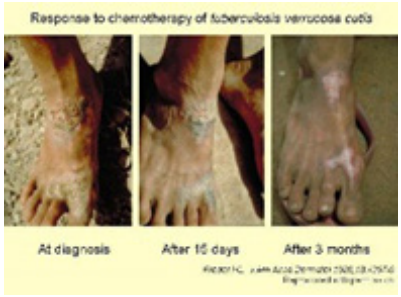
3.6 Diagnosis of Extrapulmonary TB

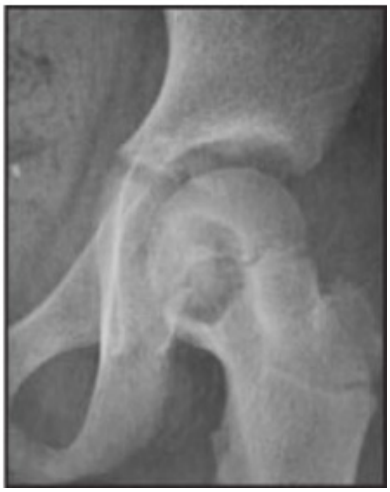
TB can affect all body tissues except the hair, nails and the teeth (enamel). The diagnosis of extra-pulmonary TB largely depends on the health worker index of suspicion as well as the ability of the health worker to conduct appropriate investigations to rule out other differential diagnoses. The tabe below is a summary of some of the common forms of EPTB and the diagnostic approaches to confirm TB diagnosis.

Table 3.6: Common Forms of Extrapulmonary TB and Diagnostic Approach

Form of Extra Pulmonary TB	Signs and Symptoms	Diagnosis
Pleural TB with Pleural Effusion 	Tuberculous pleural effusion usually presents with: • Local chest symptoms that include chest pain, Shortness of breath. • Cough and systemic symptoms including fever and night sweats. • "stony" dullness on percussion • Reduced breath sounds on the side of the effusion.	• Chest x-ray is often required to confirm the presence of the effusion. When effusion is small a supplemental lateral decubitus view or ultrasound on the suspected side of effusion may be performed. • It is also advisable, if the expertise exists, to always perform a diagnostic pleural aspiration at the minimum to distinguish pus (empyema) from "usual" effusion. Aspirated fluid should be sent to the laboratory for cytology and microbiological tests including GeneXpert and TB Culture. • 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.

Tuberculous Peritonitis and Ascites 	Tuberculous Peritonitis and Ascites usually presents with: • abdominal pain and swelling • disturbance of bowel motion i.e., constipation or diarrhea • fever.	• Ultrasonography may show matted loops of bowel with free fluid. • Peritoneal biopsy rarely done: many of these end up with a surgical biopsies during laparotomy.
Tuberculous Meningitis	This disease is often very difficult to diagnose and requires a very high index of clinical suspicion. This disease presents with: 1. Prodromal phase - mild headache, fever, malaise 2. Meningitic phase - headache, vomiting, confusion, meningismus 3. Paralytic phase - stupor, coma, seizures, hemiparesis	The diagnosis of tuberculous meningitis is made by: • Examination of cerebrospinal fluid (CSF) obtained following a lumbar puncture: • CSF stain positive for mycobacterium or CSF GeneXpert positive. • CT Scan of the brain which shows basal meningitis, tuberculomas and development of hydrocephalus.
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 (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.

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 such as tuberculomas or cerebral infarcts. • MRI with contrast and spectroscopy is superior in the diagnosis of encephalitis, tuberculoma and spinal TB . • Often it is difficult to confirm the diagnosis of brain TB and most patients are treated on an empiric basis.
TB of the skin 	• *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)

TB of the bones and Joints 	• TB can affect any bones or joints, primarily the large bones/ joints e.g hip (see pic on the left) and spine • The spine is affected in many instances with a characteristic 'gibbus' deformity of the spine.	• Diagnosis may be confirmed by bone biopsy for culture. However, in most instances, the characteristic radiographic findings with bone destruction while soft tissues are spared.
NOTE: When patients present with symptoms of TB disease and the health care worker is not able to make a diagnosis or when there are signs of severe disease, a rapid referral to the next appropriate level is highly recommended.		

3.7 Treatment of Drug Susceptible Tuberculosis

Treatment of Tuberculosis benefits both the individual patient and the community as a whole. Any health provider undertaking to treat a patient for 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.

3.7.1 Goals of TB Treatment

The overall goals of TB therapy include:

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

3.7.2 Principles of TB treatment

The principles of TB treatment include the following:

1) Never use single drugs - this increases the likelihood of selection of naturally occurring resistant mutants to *M. tuberculosis*
2) Always use drugs in combinations - using Fixed Dose Combinations (FDCs) to avoid selection of naturally occurring resistant mutants to *M. tuberculosis*
3) Drug dosage is based on weight - to achieve therapeutic drug levels in the body and prevent medication side effects
4) Drug intake should be directly observed for all patients - to ensure adherence, prevent emergence of drug resistance, assess for medication side effects and to follow clinical response closely
5) Ensure the entire treatment is taken as recommended.

3.7.3 First line Anti-Tuberculosis Drugs

Anti-TB drugs should have one of the following properties:

A. **Bactericidal** - the ability to kill the rapidly dividing, metabolically active bacilli found in the walls of cavities and in the sputum of patients with microscopy smear-positive pulmonary tuberculosis. Drugs with high early bactericidal activity such as Isoniazid will make the patient non-infectious as early as possible.

B. **Sterilization** - the ability to kill the persisting, dormant or intermittently active bacilli, responsible for relapses. Drugs with rapid sterilization ability such as Rifampicin and Pyrazinamide will lead to the shortening of treatment.

There are four drugs used in the first line treatment of TB and they include:

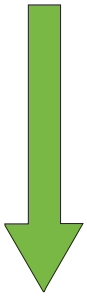
- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol

These drugs are given in two phases of treatment:

1. **Intensive phase** - lasts two months and usually consists of four drugs. Aim is to achieve a rapid killing of actively dividing bacteria, resulting in the reduction of bacillary load, negativization of sputum (within two weeks) and eradication of clinical symptoms.
2. **Continuation phase** - lasts four months to ten months and usually consists of two drugs. Aim is to kill any remaining or dormant bacilli and preventing subsequent relapse

The four drugs have differing grading of activity against M. tuberculosis as shown below.

Table 3.7: Grading of Activity of Anti-Tuberculosis Drugs

Activity	Prevention of Resistance	Early Bactericidal Activity	Sterilising Activity
High	Isoniazid	Isoniazid	Rifampicin
	Rifampicin		Pyrazinamide
		Ethambutol	
	Ethambutol	Rifampicin	Isoniazid
Low	Pyrazinamide	Pyrazinamide	Ethambutol

The four first line anti TB drugs have specific individual properties that are useful in treating the different TB bacilli populations present in any patients. These are summarized in the table below.

Table 3.8: Properties of Individual TB drugs

Drug	Mechanism of action	Target bacilli	Media	Compartment it works in
Isoniazid (H)	Bactericidal action with highest potency. Has highest early bactericidal activity and kills > 90% bacilli in the first few days of treatment.	Rapid and intermediate growing bacilli	Alkaline and acid media.	Intracellular and extracellular
Rifampicin (R)	Bactericidal action with 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. Highly potent sterilizing action and highly effective during the first 2 months of treatment.	Slowly multiplying bacilli	Acid medium	Intracellular bacilli only (macrophages)
Ethambutol (E)	Bacteriostatic. Low potency. Minimizes the emergence of possible initial resistance to Isoniazid.	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 include:

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.
5) Easier for treatment supporter to monitor treatment via DOT

Disadvantages of using FDCs include:

1) Reduced bioavailability of some drugs.
2) Flexibility in obtaining an optimal dose of some agents.
3) Difficulty in ascertaining cause of adverse drug effect when using FDCs

3.7.4 Direct Observation of Therapy

The WHO in 1993 recommended the Directly Observed Therapy Short-course (DOTS) strategy to treat TB.

DOTs helps patients to improve adherence to treatment and treatment completion, thus achieving cure and preventing the development of drug resistance. Depending on the local conditions, DOT may be undertaken at a health facility, in the workplace, in the community or at home. DOT should be provided by a treatment supporter who is acceptable and accountable to the patient and is trained and supervised by a health worker.

3.7.5 Adult TB First Line Treatment Regimens

First line anti-TB treatment regimens for use in adult patients are shown in the table below.

Table 3.9: First Line Anti-tuberculous regimen for Adult Patients

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

The following table shows weight-based dosage for first line FDC anti-TB treatment regimens.

Table 3.10: FDC treatment dosage for adults

FDC Dosages	Formulation	30-39kg	40-54 kg	55 - 69 kg	Over 70 Kg
Rifampicin 150 mg + Isoniazid 75 mg + Pyrazinamide 400 mg + Ethambutol 275 mg	4-FDC tablet RHZE	2	3	4	5
Rifampicin 150 mg + Isoniazid 75mg	2-FDC tablet RH	2	3	4	5

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 the emergence of drug resistance.
3) For children or adolescents above 30kg do not give RH 60/60 but treat as adults
4) All patients taking anti-TBs should also receive daily pyridoxine as shown in the table below to reduce the risk of developing peripheral neuropathy. However, lack of pyridoxine should not stop TB therapy.

Table 3.11: 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

3.8 Special Considerations in the Management of TB

a) Hospitalization:

Patients with TB may require hospitalization in certain circumstances as outlined below:

1) Severe forms of PTB and EPTB (e.g. TB meningitis and pleural effusion)
2) Severe malnutrition
3) Severe pneumonia
4) Other comorbidities e.g. severe anemia, severe diarrhea, etc
5) Court ordered patients to ensure adherence
6) Severe adverse reactions such as hepatotoxicity, severe cutaneous reactions

b) Steroid Therapy:

Corticosteroids have been proven in clinical trials to improve the morbidity and mortality outcomes in patients with the following conditions:

1) TB meningitis
2) TB pericarditis
3) TB Immune Reconstitution Inflammatory Syndrome in PLHIV

For TB meningitis, dexamethasone in the dose of 0.4 mg/kg/day is recommended in adults (>14 years) in conjugation with antitubercular drugs. The dose should be reduced over 6–8 weeks. In other conditions, Prednisolone is the preferred corticosteroid used.

The following table summarizes the dose of Prednisolone for adults and children which are given in a tapering dosage over 7 weeks.

Table 3.12: Dosage of prednisone for adults and children

DOSAGE	Weeks 1-4	Weeks 5-6	Week 7
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

3.9 TB Treatment Outcome Definitions

Upon treatment, persons with drug susceptible TB should be assigned a treatment outcome from the following list.

Table 3.13: Treatment Outcomes for Drug Susceptible 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.
Moved to Cat. 4 (MT4)	A patient who is confirmed to have Drug resistant TB while on first line TB treatment regimen.
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.

3.10 Complications of Pulmonary Tuberculosis

If TB is not diagnosed early and treated accordingly, a number of complications may occur. Some of the possible complications are summarized in the table below:

Table 3.13: Common Complications of Pulmonary Tuberculosis

Disease	Presentation	Management
Spontaneous Pneumothorax Presence of air in the pleural cavity resulting in impairment of oxygenation and ventilation. It is a medical emergency and results from rupture of a TB cavity adjacent to the pleura.	Acute onset of shortness of breath Chest pain	The patient should be admitted to hospital for appropriate management. Chest tube with underwater seal drainage should be performed.

Disease	Presentation	Management
It may be associated with formation of pus in the pleural space (empyema) leading to a pyopneumothorax.		Give anti-TB therapy
Bronchiectasis Chronic lung disease often secondary to an infectious process that results in the abnormal and permanent distortion of one or more of the conducting bronchi or airways. Extrinsic compression of a bronchus by enlarged nodes may cause bronchial dilation distal to the obstruction. Progressive destruction and fibrosis of lung parenchyma may lead to localized bronchial dilation.	Cough Copious amounts of sputum which is mainly greenish, blood stained and foul smelling Hemoptysis	Chest physiotherapy mainstay with postural drainage and other manoeuvers to improve drainage of respiratory secretions Infective exacerbations require antibiotics. Broad spectrum antibiotics like amoxicillin-clavulanate, metronidazole or clindamycin for anaerobic infection. Antipseudomonal antibiotics like ciprofloxacin, 3rd generation cephalosporin (Ceftazidime) should be used when colonization with *Pseudomonas* is suspected.
Lung Fibrosis Sequelae of extensive tuberculous disease with long-term lung tissue injury. Replacement of normal lung parenchyma with collagenous tissue results in changes in the lung, such as thickening and stiffening of the lung walls.	Shortness of breath, particularly with exertion Chronic dry cough Fatigue Chest pain Loss of appetite	Long term oxygen therapy in severe terminal cases Need referral to chest physicians Lung transplantation in some cases
Lung Abscess Necrosis of the pulmonary parenchyma caused by microbial infection. Seen in extensive lung damage after tuberculosis.	Fever, productive cough with putrid or sour-tasting sputum Night sweats, weight loss, and anemia Chest pain and hemoptysis	Empiric antibiotics given, aided by Gram stain and culture of sputum Broad cover for strict anaerobes and facultatively anaerobic species with any combination of a beta-lactam–beta-lactamase inhibitor eg ampicillin-sulbactam
Massive Hemoptysis Usually seen in cavitary disease and sources include the pulmonary artery, bronchial arteries, intercostal arteries, and other vessels supplying the lung. Tuberculous vascular lesions include pulmonary	Coughing up massive amounts of blood and considered to be life-threatening when there has been approximately 150 mL of blood expectorated in a 24-hour period	Ensure ABCs followed ie adequate oxygenation and ventilation, secure the airway with endotracheal tube, position the patient in lateral decubitus with bleeding side down, give fluids or blood, and

Disease	Presentation	Management
or bronchial arteritis and thrombosis, bronchial artery dilatation, and Rasmussen aneurysm.	(or 100ml/hour) or associated with airway obstruction, significantly hypoxemia or hypotension	give sylate to control bleeding. Refer for bronchoscopy by chest physician
Chronic pulmonary aspergillosis Result of colonization of tuberculous cavities or bronchiectatic lesions with the fungus A*spergilus.*	Weight loss, chronic productive cough and recurrent or persistent hemoptysis in patient previously treated for PTB Fatigue Shortness of breath Chest pain	Confirmed by high levels of serum specific Immunoglobulin G against *Aspergillus* Surgical resection is only effective treatment

3.11 Treatment Preparation, Initiation and Follow Up

3.11.1 Patient Education and Counselling

Adherence to TB treatment is essential in preventing emergence of resistance and to increase the chance of cure. This guideline provides practical steps to be used by healthcare workers to provide patient education/ counselling to patients on TB treatment.

Counselling explores and assesses psychological and emotional issues that could be pre-existing, drug induced and/or emerging in the course of the treatment due to social pressures. The approach needs to be patient-centred and geared towards helping patients find their own solutions to daily life problems that may impact negatively on adherence.

Counselling/Education will aim to achieve the following:

a) Inform and educate patients and their caregivers on TB.

b) Increase patient understanding of TB disease and treatment to enhance adherence.

c) Empower the patient to take responsibility for their treatment.

d) Identify psychological issues arising from treatment or disease presence and provide psychological support

e) Create a harmonised patient education for enhanced holistic care.

f) Improve patient/health care worker relationship

This relies on the quality of the therapeutic relationship established between the educator, the clinic team and the patient.

3.11.2 Patient Counselling and Education Before Treatment

TB patients MUST be provided with counselling and education sessions before initiation of treatment and subsequently provided during follow-up visits. The counselling will be provided by the health care workers at the TB treatment centre. The process of counselling and education will follow the steps below:

1. Create rapport and assure confidentiality.
2. Use of simple and appropriate language that the patient can understand.
3. Listen to feedback from the patient and address any questions.
4. Clarify information.
5. Explore barriers to treatment adherence.
6. Provide information on TB treatment and adherence.
7. Provide information about treatment services which include duration of treatment, possible side effects, importance of DOT, follow up visits
8. Roles and responsibilities for the patients, family, patient supporters and health care worker

3.11.3 Patient Counselling and Education During Treatment

The counselling/ education sessions will aim to develop a TB treatment plan in line with a patient-centred approach. The plan will include a schedule of clinic visits for treatment follow up and counselling/education sessions. The frequency of the visits will be weekly during intensive phase and two weekly in the continuation phase.

However, the frequency of visits for counselling/education may be increased during any phase of treatment if issues that would affect adherence are identified. The following will be conducted during the follow up counselling and education sessions as further described in Table 3.14:

- Adherence assessment, supportive education
- Psychosocial review and support
- Side effect monitoring

Table 3.14: Counselling and Education Schedule for Tuberculosis patients

Phase	Session	Content
Baseline	First contact with patient (Provide a session at the time of giving results)	• Establish rapport and assuring confidentiality • Educate patients on TB treatment and prevention; transmission, common drugs side effects • Educate on importance of referral of contacts for TB screening

Phase	Session	Content
		• Clarify information and myths • Explore barriers to treatment adherence • Provide information on TB treatment and adherence • Roles and responsibilities for the patients, family, patient supporter and health care worker
Intensive phase	At every visit (weekly) If major issues are identified, arrange for frequent adherence sessions	• Adherence assessment and support • Supportive education • Psychosocial review and support • Side effects monitoring
Continuation phase and follow-up	Every two weeks, until completion of treatment	• Adherence assessment, support and education • Side effects monitoring • Emotional validation, reassurance

3.12 Treatment Response Follow-up for bacteriologically confirmed TB

All patients should be regularly monitored to assess their response to therapy. Regular monitoring of patients also facilitates treatment completion and allows the identification and management of adverse drug reactions. All patients, their treatment supporters and health workers should be instructed to report the persistence or reappearance of symptoms of TB (including weight loss), symptoms of adverse drug reactions, or treatment interruptions.

Response to treatment in pulmonary bacteriologically confirmed TB patients is monitored by sputum smear examination as shown in the table below. Clinical visits for the patient should be booked weekly during the intensive phase and twice weekly during the continuation phase of anti-tuberculous therapy.

Table 3.15: Treatment Response Assessment for Smear positive or GeneXpert Positive Patients

Months of treatment	Specimen	Test	Result	Comment/action
2 or 3	Sputum	Microscopy	Negative	Transit to continuation phase
			Positive	• For patients who remain positive at 2 or 3 months: Evaluate for **adherence**, and other causes of **delayed conversion** and continue **RHZE** for 1 more months.

Months of treatment	Specimen	Test	Result	Comment/action
				• Request for **all** the following **drug susceptibility tests** (DST); GeneXpert, FL* LPA and SL** LPA, Culture, FL DST and SL DST. • If DST results is received by then adjust treatment regimen based on DST results accordingly
5	Sputum	Microscopy	Negative	Continue treatment until end of month
			Positive	• For patients who remain positive at 5 or 6 months - **declare treatment failure** and stop anti-TB treatment • Patient must be reviewed by the sub county and county TB clinical review teams (PMDT teams) • Evaluate for adherence, other causes of delayed sputum conversion and treatment failure • Request for GeneXpert, FL LPA and SL LPA, Culture, FL DST and SL DST • Review DST results and re-initiate treatment based on DST results and other clinical findings
6	Sputum	Microscopy	Negative with one previous sputum negative	**Declare patients cured** and enrol for the post TB lung disease care follow up clinic

** FL - First Line*

***SL - Second Line*

3.12.1 Causes of Delayed Sputum Conversion

Smear status at the end of the intensive phase is a poor predictor of which new patients will relapse. However, detection of a positive sputum smear remains important as a trigger for the patient assessment as well as for additional drug susceptibility tests as outlined in Table 3.15. The proportion of smear-positive patients with sputum smear conversion at the end of the intensive phase is also an indicator of TB programme performance. Causes of delayed sputum conversion are summarized below in Table 3.16.

Table 3.16: Causes of Delayed Sputum Conversion

Patient Factors	Bacillary Factors	Drugs Factors	HCW and Health system factors
Extensive cavitations	High pre-treatment bacillary loads - smears 2+ to 3+	Poor quality	Delayed diagnosis
Poor adherence	Resistance - first line treatment failure with positive culture	Expired drugs	Inadequate knowledge among HCWs
Under dosage	Dead / Non-viable bacilli with negative culture - possible even up to 4th to 5th month of treatment due to bactericidal action of Rifampicin and Isoniazid	Poor storage	Unavailability of guidelines
Malabsorption	Non tuberculous mycobacteria		Lab error
HIV			Poor supervision of intensive phase
Chronic diarrhea			
Diabetes mellitus			
Older age > 50 years			
Smokers			
Males			
Delayed consultation	High pre-treatment bacillary loads - smears 2+ to 3+		Poor health seeking behavior in the community

3.13 Treatment Interruption

If a patient misses an arranged appointment to receive treatment, the TB clinic should ensure that the patient is contacted within a day after missing treatment during the initial phase, and within a week during the continuation phase. The patient can be traced using the locating information previously obtained on enrolment.

It is important to find out the cause of the patient's absence so that appropriate action can be taken and treatment can continue.

Steps to take for treatment interruption include:

1. Actively trace patients back from locator information in register (phone call, home visit)

2. Establish the causes for interruption of treatment
3. Address the problem or concerns of the patients
4. Educate and counsel the patients
5. Collect sputum for GenXpert

NOTE:

When a patient refuses to continue treatment, every effort should be made to convince the patient to continue. When all measures fail and patients insist on stopping treatment, the patient should sign a refusal form so that other options are considered such as legal action since TB is a communicable disease of public health concern.

The following table shows the management of treatment interruption once the patient returns.

Table 3.17: Management of Treatment Interruption in Tuberculosis Treatment

Treatment Phase	Length of interruption	Action to be taken
Intensive Phase	**Less than 2 weeks**	1. Perform adherence counselling to address causes of treatment interruption 2. Continue treatment at the point it was stopped and add the missed doses to the intensive phase.
	More than 2 weeks	1. Perform adherence counselling to address causes of treatment interruption 2. Request for smear microscopy - If positive, restart treatment and give the full course of anti-TB treatment - If negative, continue treatment and add the missed doses to the intensive phase 3. Perform DST (GeneXpert, Culture, LPA DST) upon return for all. **If treatment is interrupted for more than 2 months** 1. Assign outcome as Lost to Follow-Up 2. Upon return, register the patient as Treatment after Loss to Follow-up (TLF) 3. Re-start anti-TB treatment
Continuation Phase	**Less than a month**	1. Perform adherence counselling to address causes of treatment interruption 2. Continue treatment at the point it was stopped and add the missed doses to the continuation phase.

	More than a month	1. Perform adherence counselling to address causes of treatment interruption 2. Request for smear microscopy - If negative, continue treatment and add the missed doses to the continuation phase. - If positive, declare treatment failure and re-start anti-TB treatment 3. Perform DST (GeneXpert, Culture, LPA DST) for all treatment interrupters **If treatment is interrupted for more than 2 months** 1. Assign outcome as Lost to Follow-Up 2. Register the patient as Treatment after Loss to Follow-up (TLF) and Perform DST as above 3. Restart anti-TB treatment

3.14 Common Adverse Effects of First Line Anti-Tuberculous Drugs

Most TB patients complete their treatment without any significant adverse drug effects. However, a few patients do experience adverse effects. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly. Routine laboratory monitoring is not necessary.

Health personnel can monitor adverse drug effects by educating patients how to recognize the symptoms of common effects, urging them to report if they develop such symptoms, and by asking about symptoms when patients come to collect drugs.

The following is the approach to the management of the most common adverse effects to first line anti-TB medicines.

a) Adverse Effect: Acute Hepatotoxicity

Causative agent: (in decreasing order of likelihood): **Pyrazinamide, Rifampicin, Isoniazid**

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
ALT (SGPT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
AST (SGOT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
ACTION	**Continue treatment regimen**. Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Continue treatment regimen.** Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Stop all drugs,** including anti-TB drugs; **measure LFTs weekly**. **Treatment may be reintroduced after toxicity is resolved.**	**Stop all drugs**, including anti-TB drugs; **measure LFTs weekly. Treatment may be reintroduced after toxicity is resolved.**

Suggested management strategy

Reintroduce anti-TB drugs once liver enzymes return to normal level. Anti-TB drugs should be reintroduced in a serial fashion by adding a new medicine every three to four days. The least hepatotoxic drugs while monitoring liver function tests after each new exposure. (E, H,R,Z).

Consider suspending the most likely offending drug permanently if it is not essential to the regimen. This is often the case for pyrazinamide if it is less likely to be effective by clinical history.

b) Adverse Effect: Peripheral Neuropathy

Causative agent: **Isoniazid**

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life-threatening
Neurosensory alteration (including paraesthesia and painful neuropathy)	*Asymptomatic with sensory alteration on exam or minimal paraesthesia causing no or minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing inability to perform usual social and functional activities*	*Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions*
Action	Monitor. If symptoms improve after 2 weeks, consider restarting these drugs. **Consider restarting Lzd at a lower dose.**	Stop Cs and Lzd (high dose H). If symptoms resolve after 2 weeks, consider restarting cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting cycloserine. **Do not reintroduce Lzd.**

Symptomatic relief for peripheral neuropathy:

- **Non-steroidal anti-inflammatory drugs** or acetaminophen helps alleviate symptoms.
- **Tricyclic antidepressants** have also been used successfully. Start amitriptyline 25 mg at bedtime. The dose should be increased to a maximum of 150 mg daily for refractory symptoms.
- **Carbamazepine** is effective in relieving pain and other symptoms of peripheral neuropathy.

c) Adverse Effect: Optic Neuritis

Causative agent: **Ethambutol**

	Grade 1 Mild	Grade 2 Moderate	Grade 3 severe	Grade 4 life-threatening
Visual changes (from baseline)	*Visual changes causing minimal or no interference with usual social and functional activities*	*Visual changes causing greater than minimal interference with usual social and functional activities*	*Visual changes causing inability to perform usual social and functional activities*	*Disabling visual loss*
Action	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**

Suggested management strategy

- Do not restart the suspected causative drug (Linezolid or Ethambutol)
- Refer patients to an ophthalmologist for further evaluation and management.
- Optic neuritis generally improves following cessation of offending drug, if it can be stopped early enough.

3.15 Dietary Considerations for Persons on First Line Anti-TB Medicines

Drug Name	Dietary Restriction	Possible side effect
Rifampicin	To be taken 1 hr before or 2 hrs after food.1 hr before Antacids. Avoid Alcohol	Nausea, Vomiting, Appetite loss
Isoniazid	Taken 1 hr before or 2 hrs after food. Give 50mg of Pyridoxine daily. Avoid alcohol	Hepatotoxicity, Cutaneous hypersensitivity, Peripheral Neuropathy
Ethambutol	May be taken with food. Avoid Alcohol	Anthralgia,Retrobulbar neuritis.
Pyrazinamide	May be taken with food	Hepatotoxicity, Anthralgia, Nausea, Vomiting

TUBERCULOSIS IN CHILDREN

4

KEY HIGHLIGHTS:

Background

- **1.2 million** children became ill with TB in 2019
- Children represent **10-15%** of all TB cases and this could be higher in high burden countries
- TB in young children is often disseminated and rapidly progressive

Signs and Symptoms of TB

The most common symptoms associated with TB include the following:

- Cough
- Fever and/or night sweats
- Weight loss or Poor weight (Failure to thrive)
- Lethargy/ reduced play/ less active

Diagnosis of TB in children

- The diagnosis of TB in children relies on a good history and a careful physical examination
- It is critical to establish a history of contact with an adolescent or adult with confirmed or presumptive TB within the last two years
- The diagnosis of TB can be made with confidence in the majority of children using clinical assessment/algorithm for diagnosing TB in children.
- Treatment with anti-TB drugs as part of diagnosis (trial-of-therapy) is not recommended

An attempt should be made towards obtaining a sample for GeneXpert testing, however, ***a negative Xpert MTB/RIF test result doesn't indicate the child has no TB;*** *further clinical evaluation is needed to make a clinical diagnosis of TB in such children*

Treatment of TB in children

- Use child-friendly formulations
- All children on TB treatment MUST be on pyridoxine
- Dosing for children must be weight-based and regularly adjusted to weight.

4.1 Introduction

4.1.1 Epidemiology of TB in Children

In 2019, 1.2 million children below the age of 15 years became ill with tuberculosis (WHO). Children represent 10-15% of all TB cases and this could be higher in high burden countries. Children below 5 years are more vulnerable to developing TB disease. They have paucibacillary disease and often present with non-specific symptoms. Child contacts with household exposure are 17 times more likely to be infected with TB than non-contacts.

In 2018 children accounted for 10.4% (10,051) of total TB cases notified in Kenya. About half of these were below 5 years. Approximately 21% of patients 5-14 years were co-infected with HIV. About 65% of children seeking care with symptoms are missed. Health workers need to have a high index of suspicion to improve the diagnosis of TB in children.

In the context of this guideline, a child refers to a person aged 0 to 14 years. This may differ from the definition of children in other contexts.

4.1.2 Risk of Latent TB Infection Progressing to TB disease

Children with latent TB infection can progress to active TB disease. Risk factors for this progression include:

- HIV infection
- Age especially those under the age of two years
- Recent infection with M. tuberculosis (within the last two years)
- History of previously poorly treated TB
- Immunosuppressive therapy
- Other immune suppressive conditions e.g. diabetes, silicosis, malignancies

Progression of the primary complex may lead to enlargement of hilar and mediastinal nodes with resultant bronchial collapse. Progressive primary TB disease may develop when the primary focus cavitates and organisms spread through contiguous bronchi. Lympho-haematogenous dissemination, especially in children, may lead to milliary TB when caseous material reaches the bloodstream from a primary focus or a caseating metastatic focus in the wall of a pulmonary vein. TB meningitis may result from hematogenous dissemination.

The bacilli may remain dormant in the lungs for several months or years. A positive tuberculin skin test (TST) or Interferon Gamma Release Assay (IGRA) where available would be the only evidence of infection.

TB in young children is often disseminated and rapidly progressive

4.2 Diagnosis of TB in children

The diagnosis of TB in children relies on a good history, a careful physical examination as well as relevant investigations. All efforts should be made to get a specimen for bacteriological confirmation of TB in children. **In cases where it is not possible to obtain a specimen in a timely way, this should not be a barrier to making the diagnosis, a clinical diagnosis can be made using the pediatric diagnostic algorithm.**

A trial treatment with anti-TB drugs is not recommended as a method of diagnosing TB in children. Most children with TB have Pulmonary TB. However, approximately 30 – 40% of children with TB have TB in organs outside of the chest – also called extra-pulmonary TB.

4.2.1 Diagnosis of Pulmonary TB

History

The key elements of history are:

a) History of contact with an adolescent or adult with confirmed or presumptive TB within the last two years

Close contact is defined as a person who has confirmed or presumptive TB living in the same household or in frequent contact with the child (e.g. caretakers, school staff)

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 who develop TB, do so within two years of exposure.

b) History of symptoms suggestive of TB

The most common symptoms associated with TB include the following:

- Cough
- Fever and/or night sweats
- Weight loss/Poor weight gain (Failure to thrive)
- Lethargy/ reduced play/ less active

The diagnosis of TB in children relies on a careful history and physical examination

Physical examination

a) General examination

Examine the child and check for:

- Temperature > 37.5 (fever)
- Weight (to confirm poor weight gain, weight loss)
- Respiratory rate (fast breathing).

b) Examination of the Respiratory System

In the early stages of pulmonary TB, the respiratory exam may show few abnormal signs. As the disease progresses respiratory signs become more obvious as follows:

- Cough
- Increased respiratory rate (fast breathing)
- Respiratory distress e.g. laboured breathing, chest in-drawing (this shows severe disease)
- Percussion note - dull when lobar consolidation is present (normal resonance may be found in many children with PTB).

Auscultation may be normal in early disease and abnormal in more advanced disease (crackles, bronchial breathing).

The classic symptoms of PTB are cough, fever, poor weight gain, and lethargy/ reduced playfulness

The following is a summary of the algorithm for the diagnosis of TB in children

Table 4.1: Algorithm for the diagnosis of pulmonary TB in children

History of Presenting illness	For all children presenting to a health facility ask for the following suggestive symptoms: **(Cough, fever, poor weight gain, lethargy or reduced playfulness)** Suspect TB if a child has two or more of these suggestive symptoms Ask for history of contact with adult/adolescent with chronic cough or TB within the last 2 years
Physical Examination	Examine the child and check for: • Temperature >37.5 (fever) • Weight (to confirm poor weight gain, weight loss) - check growth monitoring curve • Respiratory rate (fast breathing) • Respiratory system examination - any abnormal findings# Examine other systems for abnormal signs suggestive of extra-pulmonary TB+

Investigations	Obtain specimen* for Xpert MTB/RIF (and culture when indicated**) Do a chest X-ray (where available) Do a Mantoux test*** (where available) Do an HIV test Do other tests to diagnose extra-pulmonary TB where suspected+	
Diagnosis	**Bacteriologically confirmed TB:** Diagnose if specimen is positive for MTB	**Clinically diagnosed TB:** *Child has* **two or more** *of the following suggestive symptoms:* • Persistent cough, fever, poor weight gain, lethargy PLUS **two or more** of the following: • Positive contact, abnormal respiratory signs, abnormal CXR, positive Mantoux Note: If the child has clinical signs suggestive of EPTB, refer to EPTB diagnostic table+
Treatment	**Treat for TB as follows:** • All children with **bacteriologically confirmed TB** • All children with a **clinical diagnosis of TB** NB: In children who do not have an Xpert result, or their Xpert result is negative, **but** they have clinical signs and symptoms suggestive of TB they should be treated for TB. All forms of TB (Except TB meningitis, bone, and joint TB): **Treat for 6 months (2 RHZE / 4 RH)** TB meningitis, bone, and joint TB: **Treat for 12 months (2 RHZE/ 10 RH)**	

**Specimen may include expectorated sputum (child > 5 years), induced sputum, nasopharyngeal aspirate, gastric aspirate, and stool. Attempt to obtain specimen in every child*

***Do culture and DST for the following children:*

1. *Rifampicin resistance detected by the Xpert test*
2. *Refugees and children in contact with anyone who has Drug-Resistant TB*
3. *Those not responding to TB treatment*
4. *Those with Indeterminate Xpert results*

**** This may include IGRA in facilities where it is available*

 # Use IMCI guidelines to classify severity of disease

+Refer to Table 4.3 on diagnosis of Extra-pulmonary TB

The diagnosis of TB can be made with confidence in the majority of children using clinical assessment

A negative Xpert MTB/RIF test result does not rule out TB.

Some children may present with an atypical clinical presentation of pulmonary TB. Some of the atypical presentations include,

a) Acute severe pneumonia

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

In this case, presume Pulmonary TB if the child does not respond to antibiotics. For a child who is HIV infected, rule out other HIV-related lung diseases e.g. PCP before considering TB treatment

b) Wheeze

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

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

Normal respiratory clinical findings do not rule out PTB.

Differential Diagnosis for Child with Chronic Cough/Respiratory Symptoms

Other conditions to consider in a child with chronic cough/chronic respiratory symptoms who does not fulfill the classical clinical picture of PTB include those in the table below:

Table 4.2: Differential diagnosis for chronic cough/respiratory symptoms

Differential 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
Gastroesophageal reflux disease	Recurrent cough/wheeze Onset in early infancy +/- Hoarse voice
Bronchiectasis	Severe persistent c o u g h, much sputum (often infected green or yellow in color) Finger clubbing CXR shows a reticular or honey-comb pattern
Congenital Heart Disease	Easily fatigability, breathlessness, Onset early infancy
Acquired heart disease	Older children, palpitations, easy fatigability, dyspnea on exertion +/- edema
Congenital respiratory disorders	Onset early infancy Commonly premature baby Noisy breathing during inspiration not responding to bronchodilators

4.2.2 Diagnosis of Extra Pulmonary Tuberculosis (EPTB)

Approximately 30-40% of children with TB have TB in organs outside of the chest – also called extra-pulmonary TB. Younger children and children with HIV disease are more likely to have EPTB than older children and adults.

EPTB disease is TB outside the lung parenchyma. It can be:

- **Intra-thoracic (inside the chest, but outside of the lung tissue) –** pleural effusion, intra-thoracic lymphadenopathy (mediastinal, paratracheal, or hilar lymphadenopathy)
- **Extra-thoracic (outside the chest) –** peripheral lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

The most common site for EPTB is the lymph nodes (hilar or cervical), followed by TB meningitis. Frequently, a child will have a combination of both pulmonary and extrapulmonary TB, with infection starting in the lungs and disseminating to other parts of the body.

History

For children suspected to have EPTB, two elements of history are important:

- History contact with an adolescent or adult with confirmed or presumptive TB within the last two years
- History of symptoms suggestive of EPTB

Children with EPTB may have the classic symptoms suggestive of TB:

- Fever and/or night sweats
- Poor weight gain or weight loss
- Lethargy, less active, reduced play
- Cough

In addition, they may have symptoms specific to the site of EPTB for example:

- Swollen neck lymph nodes may be discharging caseous material
- Symptoms of meningitis – progressive unrelenting headache, irritability, confusion, focal neurologic weakness, convulsions, reduced consciousness
- Symptoms of hilar lymphadenopathy compressing the airways – Wheeze, rapid breathing, and worsening breathlessness (may or may not have cough)

Table 4.3: Some of the sites EPTB may affect their presentation and investigations

Site of EPTB	History	Clinical signs	Investigation
Cervical Lymphadenitis (TB adenitis)	• Progressive swelling in the neck • Usually on one side, but may occur on both sides • Several swellings that are not painful with or without thick yellow discharge • May or may not have cough	• Enlarged cervical LN >2cm diameter Not hot or tender+/- • Discharging sinus (caseous discharge) • Most common in the neck area • Tachypnea • +/- respiratory distress • Normal percussion note	1. Fine needle aspiration when possible 2. Mantoux
Hilar lymphadenopathy	• Noisy breathing (parent may describe as a wheeze) • Fast breathing, progressive breathlessness	• Breath sounds may be louder on one side of the chest than on the other • Wheeze/rhonchi which are often asymmetric, low pitched, with poor response to bronchodilators	1. CXR 2. Mantoux
Pleural TB	• Chest pain on the affected side • Progressive breathlessness • May or may not have cough	• Dullness on percussion • Reduced breath sounds on the affected side	1. CXR 2. Pleural tap 3. Mantoux test

Site of EPTB	History	Clinical signs	Investigation
TB meningitis	• Unremitting headache progressing to Irritability/abnormal behavior • Lethargic/ reduced level of consciousness with or without Convulsions	• Irritability/abnormal behavior • Lethargic/reduced level of consciousness, with or without convulsions • Neck stiffness • Bulging fontanel • Cranial nerve palsies	1. Lumbar puncture to obtain CSF 2. Infants-cranial ultrasound 3. Older child do CT scan head 4. Mantoux test
Miliary TB	• Non-specific • Lethargic • With or without cough	• Fever • Wasting • With or without respiratory signs • With or without hepatosplenomegaly	1. CXR 2. Mantoux test
Abdominal TB	• Painless abdominal swelling • With or without GIT disturbances	• Ascites • With or without hepatosplenomegaly	1. Ascitic tap 2. Abdominal ultrasound 3. Mantoux test
Spinal TB	• Painless deformity of the spine • May have lower limb weakness/paralysis	• Gibbus deformity • X-ray shows anterior vertebral collapse	1. Lateral X-ray spine 2. Mantoux test
Pericardial TB	• Cardiac failure: Cough, difficulty in breathing, swelling of legs and/or abdomen	• Apex beat difficult to palpate • Muffled heart sounds	1. CXR 2. Echocardiogram 3. Mantoux test
TB bone and joint (excluding spine)	• Painless swelling end of long bones with limitation of movement Painless unilateral joint swelling	• Effusion of large joints (usually knee or hip) • Limitation of movement in long bones	1. X-ray 2. CT scan 3. MRI

The most common form of extra-pulmonary TB in children is lymphadenopathy. This can be cervical or hilar

Investigations

Having taken a comprehensive history and conducted a thorough physical examination, a Mantoux test/IGRA may be done where applicable to determine exposure. A chest x-ray should also be done where accessible to aid diagnosis. Samples should be collected for GeneXpert testing (where applicable). Sputum induction and gastric lavage are encouraged for younger children who cannot produce sputum.

Table 4.4: Laboratory Tests, Targets, and Purpose

Laboratory test	Target	Purpose
Immunologic Tests		
Tuberculin skin test	• Children	• Useful test to detect TB exposure in children and support presumptive clinical diagnosis in situations where there is no obvious close TB contact to the child
Interferon-gamma release assay (IGRA)	• Children	• Similar role to TST but more expensive
Radiological investigations		
X-ray	• Chest X-ray for all infants, children, and adolescents with presumptive TB • X-rays of the affected bone, joint, spine as appropriate	• Diagnosis of TB and EPTB in all children where x-ray services are available. • **For children obtain Anteroposterior and lateral CXR views**
Ultrasound	• Abdominal ultrasound Chest ultrasound	• Diagnosis of abdominal TB Detection of pleural effusion
CT Scan or MRI	• Head CT, Chest CT as needed • MRI of the abdomen, head, chest, or spine • as needed	• Evaluation of severe or complicated cases
Bacteriological Investigations		
MTB/RIF GeneXpert	• The first-line test for all presumptive or suspected TB in Infants, children, and adolescents • Surveillance for Drug-Resistant TB among children previously treated for TB, child contacts of DRTB patients, refugees, prisoners, children not improving on first-line TB treatment	• For diagnosis of TB • To determine rifampicin susceptibility • Done for child specimens of sputum, CSF, Gastric aspirate, Pleural fluid, pericardial fluid, Ascitic fluid, stool

Smear microscopy (Fluorescent and Light microscopy)	• Infants, children, and adolescents with presumptive Pulmonary TB	• Only used in situations where Xpert is not accessible • Monitoring smear-positive and/or GeneXpert positive TB patients on treatment at months 2, 5 and 6
Whenever possible try to make a bacteriological diagnosis of TB in infants and older children by obtaining specimens and sending them for Gene Xpert (preferred first-line test), AFB microscopy, or TB culture.		

Immunologic Tests

Tuberculin Skin Test (Mantoux test)

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 a Mantoux test is very important. *(Refer to appropriate SOP)*

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).

Interferon-Gamma Release Assays (IGRAs)

Haematological tests that can aid in diagnosing Mycobacterium tuberculosis infection e.g. QuantiFERON®-TB Gold In-Tube test (QFT-GIT) and T-SPOT®.*TB* test (T-Spot). It is an antibody-antigen test that - like the Mantoux test - measures the presence of an immune response to TB bacilli. There is limited data on its use in:

- Children younger than 5 years of age
- Persons recently exposed to M. tuberculosis
- Immunosuppressed persons and
- Serial testing.

NOTE:

- ***Correct technique of administering, reading, and interpretation of the Mantoux test is very important (Refer to appropriate SOP)***
- ***A negative Mantoux does not rule out TB (especially in the HIV positive or malnourished child)***
- ***Mantoux test may be negative despite the child having TB especially in severe disseminated TB, malnutrition, and HIV disease***

A child in close contact with a smear-positive household member should be considered TB infected and TST/IGRA may not be necessary

Chest Radiograph (Chest X-ray)

The chest radiograph (chest x-ray) is an important investigation for the diagnosis of TB in children. A clinical diagnosis of PTB may be made by combining suggestive history, physical examination findings, and an abnormal CXR. Primary TB tends to be predominantly enclosed in hilar lymph nodes and therefore the bacilli are absent in sputum. In this case, the CXR provides important support for making a clinical diagnosis of PTB in children.

For children with history and physical signs suggestive of TB, it is important to do a chest x-ray.

An abnormal CXR provides additional evidence to support the clinical diagnosis of PTB in children.

The radiological features that may be suggestive of PTB include:

- Enlarged hilar or subcarinal lymph nodes (check for these on AP and lateral views of the chest x-ray)
- Lung opacification – especially if focal (segmental or lobar opacification common, but in infants may be patchy opacification in many lobes as seen in broncho-pneumonia)
- Diffuse micronodular infiltrates throughout both lungs (milliary pattern)
- Older children and adolescents – upper lobe opacification with or without cavities.

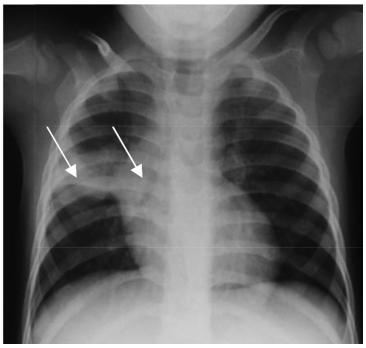
Other radiological features may be suggestive of EPTB:

a) In the thoracic cavity, e.g. Pleural effusion (usually one-sided)

b) Other sites in the body e.g. bone and joint disease, spinal TB

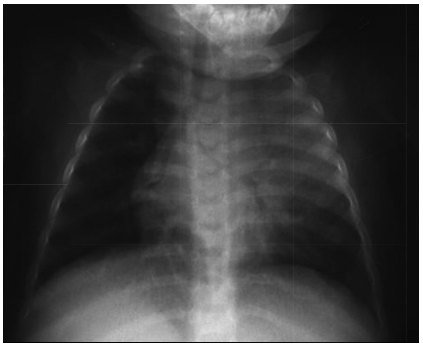
The images below show some of the radiological changes that may occur with PTB.

Figure 4.1 Pictures suggestive of Pulmonary TB

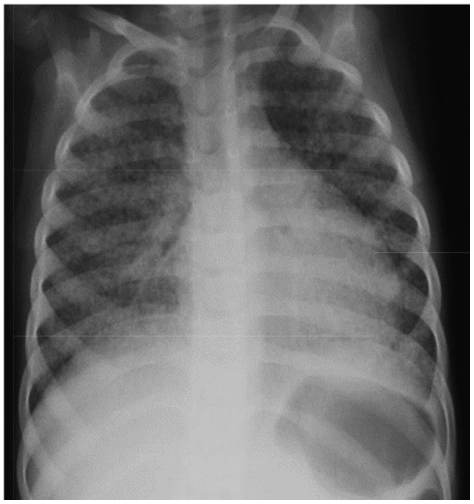


a) Right perihilar lymph node enlargement

With opacity in the right mid-zone

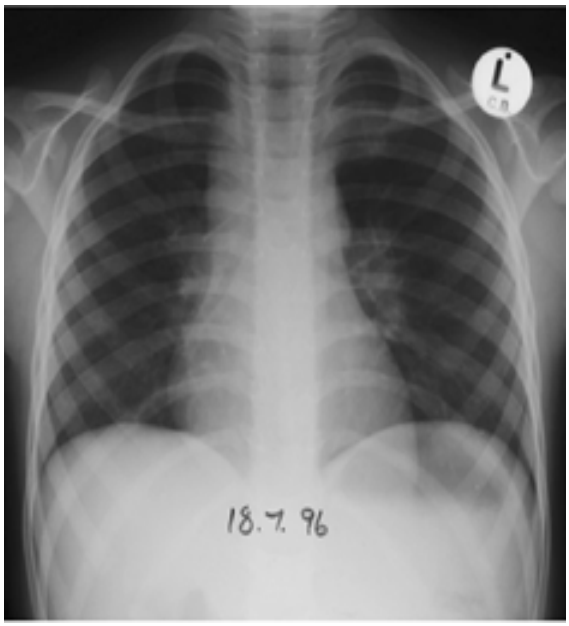


b) Left upper lobe opacification with narrowing and shift of left main bronchus

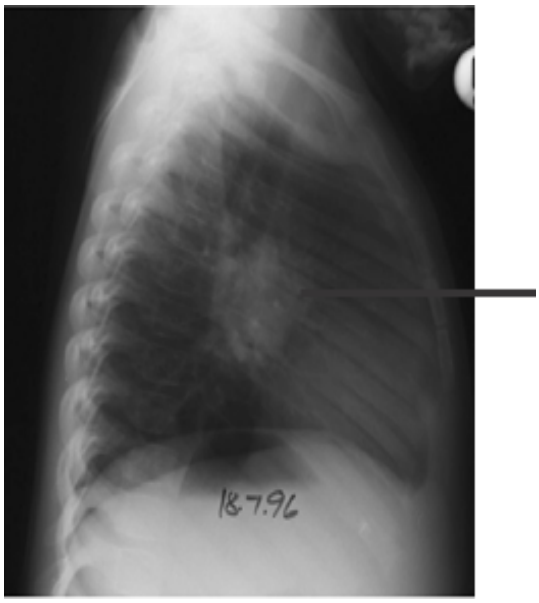


c) Miliary TB: Typical bilateral diffuse micro nodular pattern.

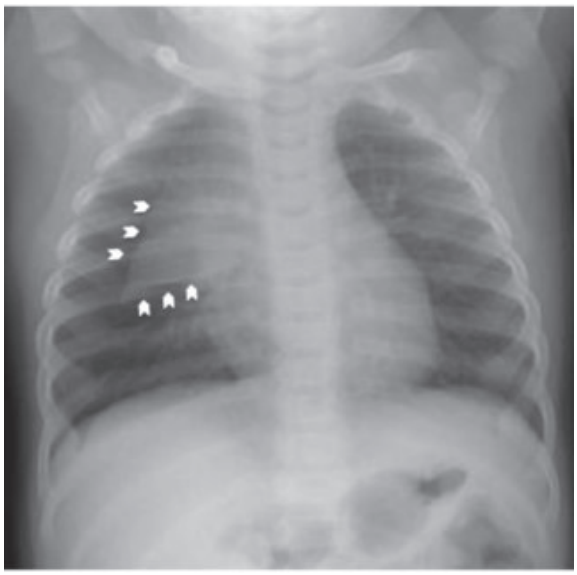
Figure 4.1 Pictures suggestive of Pulmonary TB



d-1) In suspected hilar and paratracheal lymph (node) gland enlargement, the diagnosis can be made with more certainty when a lateral chest radiograph is examined as well. This should not be confused with mediastinal widening due to a large thymus (see figure 4.1-e)



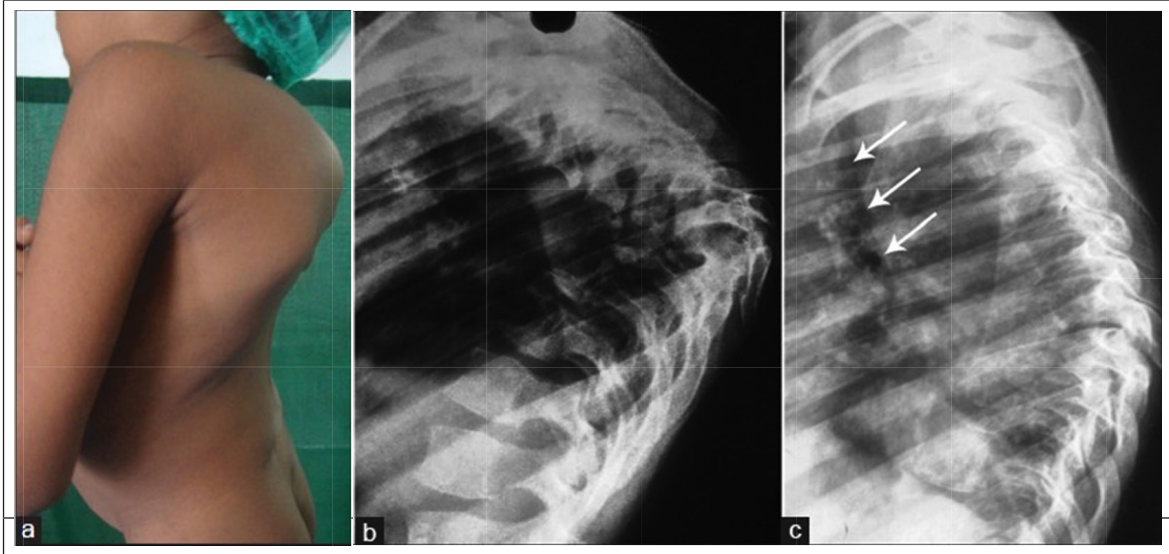
d-2) Massive hilar lymph gland enlargement visible on the lateral chest radiograph. The arrow indicates the hilar lymph glands



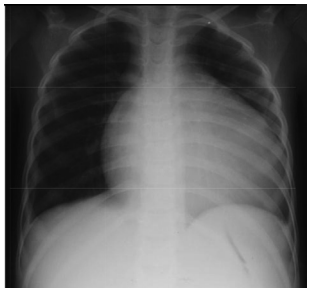
e) Common cause for a widened mediastinum in a young child is a large thymus which causes the sail sign on the chest radiograph (see arrowheads)

Radiological features that may suggest extrapulmonary TB vary according to the affected site. Examples include these below:

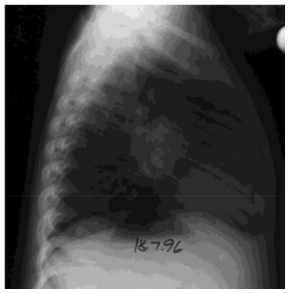
Figure 4.2 X-rays suggestive of extrapulmonary TB



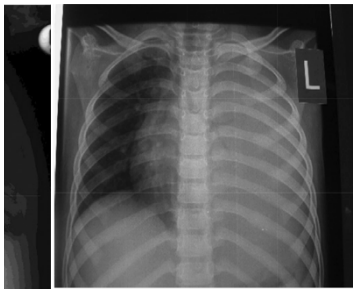
a-c) Spinal TB: collapse of thoracic vertebra causing angulation in a 6-year old boy



d) Lateral CXR showing enlarged hilar lymph nodes ("doughnut sign")



e) TB pleural effusion: large left-sided effusion. Pleural tap to differentiate from emphysema



f) Pericardial TB: enlarged cardiac shadow. Echo-cardiogram to differentiate from other causes of cardiac failure

Other Tests for TB diagnosis

1. Radiologic tests include:
   - CT scan – In complicated intracranial TB (tuberculoma, hydrocephalus, comatose child)
   - Ultrasound – useful for abdominal TB and pleural effusion
2. Laboratory tests: These are mainly used in research settings
   - Nucleic acid amplification tests (NAAT)
3. Nonspecific tests like ESR and C- reactive protein tests suggest the presence of inflammation if increased.

4. Biochemical tests – Elevated protein and low glucose levels in cerebrospinal fluid (CSF), pleural aspirates, or ascitic aspirates suggest an exudate**.**

GeneXpert MTB/Rif/Ultra: Where accessible, this is the preferred test for diagnosis of TB among children. The GeneXpert test can be performed for Sputum, gastric/ nasopharyngeal aspirate, bronchial secretion specimens, CSF, ascitic fluid, pleural fluid, and stool. Specimens from children who cannot expectorate can be obtained through a gastric aspirate or sputum induction *(Refer to appropriate SOP).*

A negative Xpert MTB/RIF test result however doesn't indicate the child has no TB; further clinical evaluation is needed to make a clinical diagnosis of TB in such children.

Other tests may be used together with those above to further support a diagnosis of TB. These are shown in the table below:

Table 4.5: Adjunct test for use in selected situations

Laboratory Test	Target	Purpose
Line Probe Assay (LPA)	Children who are: • MTB positive rifampicin sensitive, and are at high risk for DRTB • MTB positive rifampicin-resistant, regardless of DRTB risk profile	To determine if Isoniazid resistance is present
Culture and DST	Children who are: • Eligible for LPA should also have a culture and DST requested • Children with clinically suspected TB whose Xpert is negative • Children who are on treatment for TB who are failing to respond to therapy	To diagnose TB To determine the drug sensitivity pattern To diagnose infections with non-tuberculous mycobacteria
Histology	All presumptive extra-pulmonary TB where FNA is indeterminate	Tissue diagnosis in suspected EPTB e.g. TB adenitis

HIV test

Making a diagnosis of HIV infection has obvious implications for the management of TB and HIV. All children with suspected TB should be tested for HIV.

4.3 Treatment of Drug Sensitive Tuberculosis in Children

Treatment outcomes in all children are generally good provided treatment is started as soon as a diagnosis is made. However, response to treatment in HIV positive children may be slow. Children generally tolerate anti-TB medicine better than adults and their dosages are calculated according to weight (not age). Weight is important for monitoring treatment response.

The goals of anti- TB treatment in children are to:

- Cure the child of TB
- Prevent death from TB
- Prevent complications arising from TB disease
- Prevent TB relapse/recurrence by eliminating the dormant bacilli
- Prevent the development of drug resistance by using a combination of drugs
- Reduce TB transmission to others

4.3.1 Standard Operating Procedures for Treatment

- Treatment should start as soon as diagnosis is made (bacteriological confirmation or clinical diagnosis).
- Classify the patient based on the site of TB disease before starting treatment (Pulmonary TB or extrapulmonary TB).
- Identify a treatment supporter (Caregiver) for all ages including older children.
- Adherence to the full course of treatment should be emphasized and reinforced
- Breastfeeding infants and children should continue while receiving TB treatment.
- Treatment outcomes in children are generally good even in the HIV infected provided treatment is started promptly. However, response to treatment in HIV co-infected children may be slow.
- Children generally tolerate anti-TB drugs better than adults.
- Weight is important for monitoring treatment response therefore must be taken and recorded at every visit.
- Record the TB diagnostic category, treatment regimen, and date anti-TB treatment was started on the road-to-health book as well as on TB record card and facility TB register.
- Calculate drug dosages at **every visit** according to the child's current weight (note that children gain weight while receiving anti-TB treatment). **Doses should be adjusted according to weight. In case of weight increase then the dose should be increased according to the weight band and reduced accordingly when weight decreases. In instances of weight loss evaluate the child further to establish the cause and manage accordingly.**

- Once treatment is started it must be completed; **"trial of TB treatment" should never be used as a diagnostic tool.**

4.3.2 Recommended Treatment Regimen

Dosages for paediatric TB treatment (child-friendly formulations)

- During the intensive phase, give paediatric FDC of RHZ dispersible tablets plus E tablets.
- During the continuation phase, give paediatric FDC of RH dispersible tablets.

The table below shows the current recommended TB treatment regimen in children

Table 4.6: 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 and *Osteoarticular TB*	2 RHZE	10 RH
Drug-resistant TB	Refer to a DR TB specialist and inform CTLC	

**H=Isoniazid, R= Rifampicin, Z=Pyrazinamide, E= Ethambutol*

Table 4.7: Dosage of individual first-line anti-TB drugs according to body weight

Drug	Recommendations Average dose in mg/kg	Range in mg/kg	Maximum Dose
Isoniazid	10	7–15	300mg
Rifampicin	15	10–20	600mg
Pyrazinamide	35	30–40	2.0g
Ethambutol	20	15–25	1.0g

The first 3 drugs (Isoniazid, Rifampicin, and Pyrazinamide) have been combined into paediatric child-friendly fixed-dose combinations (FDCs) which are dispersible in liquid, have a pleasant taste, and are therefore easier for children to take. The improved paediatric TB FDCs provide the correct dosing ratio of Rifampicin: Isoniazid: Pyrazinamide as follows:

Rifampicin 75mg: isoniazid 50mg: pyrazinamide 150mg **(RHZ 75:50:150)** tablet

Rifampicin 75mg: isoniazid 50mg **(RH 75:50)** tablet

Ethambutol is available as a single drug paediatric tablet of 100mg **(E 100).** 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 bactericidal levels.

Ethambutol can be safely used in all children at the recommended dosage of 20mg/kg

Table 4.8: Dosages for a child weighing up to 3.9 kg

Weight band (Kg)	Number of tablets				
	Intensive Phase			Continuation Phase	
	RHZ (75/50/150mg)	E (100mg)	How to reconstitute the medicines	RH (75/50mg)	How to reconstitute the medicines
Less than 2 Kg	¼	¼	Dissolve **one (1)** tablet of RHZ in **20 ml** of safe drinking water. Once fully dissolved, add the completely crushed **one (1)** tablet of Ethambutol and give **5ml (1/4)** of this solution measured with a syringe.	¼	Dissolve **one (1)** tablet of RH in **20 ml** of safe drinking water. Once fully dissolved, give **5ml (1/4)** of this solution measured with a syringe.
2 – 2.9	½	½	Dissolve **one (1)** tablet of RHZ in **20ml** of safe drinking water. Once fully dissolved, add the completely crushed **one (1)** tablet of Ethambutol and give **10ml (1/2)** of this solution measured with a Syringe.	½	Dissolve **one (1)** tablet of RH in **20 ml** of safe drinking water. Once fully dissolved, give **10ml (1/2)** of this solution measured with a Syringe.

Weight band (Kg)	Number of tablets				
	Intensive Phase			Continuation Phase	
	RHZ (75/50/150mg)	E (100mg)	How to reconstitute the medicines	RH (75/50mg)	How to reconstitute the medicines
3 – 3.9	¾	¾	Dissolve **one (1)** tablet of RHZ in **20 ml** of safe drinking water. Once fully dissolved, add the completely crushed **one (1)** tablet of Ethambutol and give **15ml (3/4)** of this solution measured with a syringe.	¾	Dissolve **one (1)** tablet of RH in **20 ml** of safe drinking water. Once fully dissolved, give **15ml (3/4)** of this solution measured with a syringe.

Ethambutol is not dispersible. Crush it completely before adding it to the prepared solution of RHZ during the intensive phase.

After giving the child their dose for that day, discard the rest of the solution. Prepare a fresh solution every day.

Table 4.9: Dosages for a child weighing 4-25 kg

Weight band (Kg)	Number of tablets				
	Intensive Phase			Continuation Phase	
	RHZ (75/50 /150mg)	E (100mg)	How to reconstitute the medicines	RH (75/50mg)	How to reconstitute the medicines
4 - 7.9	1	1	Dissolve the tablet(s) of RHZ in **20 ml** of safe drinking water. Once fully dissolved, add the completely crushed tablet(s) of Ethambutol and give **ALL** this solution to the child.	1	Dissolve the tablet(s) of RH in **20 ml** of safe drinking water. Once fully dissolved give **ALL** this solution to the child.
8 - 11.9	2	2		2	
12 - 15.9	3	3		3	
16 - 24.9	4	4		4	
25 kg and above	Use adult dosages and preparations				

Table 4.10: Dosages for a child weighing 25kgs and above (adult formulation dosage table)

Weight band (Kg)	Number of tablets	
	Intensive Phase	Continuation Phase
	RHZE (150/75/400/275mg)	RH(150/75mg)
25 – 39.9	2	2
40 – 54.9	3	3
55kg and above	4	4

Use of Ethambutol in children

The risk of toxicity is negligible when Ethambutol is used at recommended dosages of **20(15-25) mg/kg/day.**

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

Pyridoxine supplementation for children on TB treatment

Isoniazid is associated with a potential adverse effect of peripheral neuropathy. Children who are malnourished or who have borderline to low levels of pyridoxine (vitamin B6) are most at risk of developing this adverse reaction to INH.

ALL children who are on an Isoniazid-containing regimen should be given pyridoxine throughout treatment, to prevent/minimize the risk of Isoniazid toxicity.

The recommended doses of pyridoxine are given in the table below:

Table 4.11: Pyridoxine (vitamin B6) dosing for children on TB treatment

Weight band (Kgs)	Dose in mg	Number of 25mg tablets	Number of 50mg tablets
Less than 5	6.25 mg	Half a tablet 3 TIMES PER WEEK	Not suitable for the young infant
5.0 – 7.9	12.5 mg	Half a tablet daily	Half of 50mg tablet 3 TIMES PER WEEK

Weight band (Kgs)	Dose in mg	Number of 25mg tablets	Number of 50mg tablets
8.0 – 14.9	25 mg	One tablet daily	Half of 50mg tablet daily
15 kg and above	50 mg	Two tablets daily	One 50mg tablet daily

All children on TB treatment MUST be on pyridoxine throughout their treatment, to prevent/minimize the risk of Isoniazid toxicity

Other important observations to note include:

- Report all children receiving anti-TB treatment to the National TB Program
- Side effects may occur but are not common. The most important side effect is hepatotoxicity

4.3.3 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 comorbidities e.g. severe anaemia
- Social or logistic reasons to ensure adherence.
- Severe adverse reactions such as hepatotoxicity.

b) Steroid Therapy

Steroid therapy should be given in the following situations:

- TB meningitis and other forms of intracranial TB
- PTB with respiratory distress
- PTB with airway obstruction by hilar lymph nodes (asymmetrical wheeze)
- 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:

- The child has severe disease
- Diagnosis is uncertain
- Need for HIV-related care to commence ART
- Failure to respond to treatment despite good adherence

4.3.4 When to Stop TB treatment

Treatment should stop when:

1. There is an adverse drug reaction
2. The child develops DR-TB while on DS-TB treatment
3. The child's condition deteriorates

4.3.5 Follow-up of a Child on Anti-TB Therapy

This is a critical component for effective TB treatment. Patients should visit the health facility weekly during the intensive phase and every two weeks during the continuation phase. During the visit, the child should be assessed as shown below:

Table 4.12: Follow-up assessment

Month	Baseline	1	2	3	4	5	6	7	8	9	10	11	12
Clinical review for both PTB and EPTB (symptom assessment, drug toxicity, and adherence)	☐	Every week		Every two weeks									
Weight (dose adjustment)	☐	Every week		Every two weeks									
Height/Weight for Height Z-score/BMI for age	☐						☐						☐

Month	Baseline	1	2	3	4	5	6	7	8	9	10	11	12
Xpert MTB/ RIF (Done for diagnosis. May repeat at any other point if drug resistance is suspected)	☐												
Smear for follow up in bacteriologically confirmed TB			☐			☐	☐						
Culture and DST (if not improving/ suspected resistance)	See algorithm												
Viral load (for HIV infected)	☐						☐						☐
CXR	☐	Repeat if not responding to treatment at any point											

4.3.6 Poor Response to Treatment

Most children with TB will start to show signs of improvement within a month 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.

Potential causes of poor response to treatment include:

- Poor adherence is the commonest cause of poor response to treatment. If uncertain, a child can have a healthcare 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, etc.

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

a) If smear-positive at baseline and remains so up to 5 months

b) There is no symptom resolution or symptoms are getting worse. In this case, always confirm that adherence is good. If uncertain, a child can have a health care worker DOT at the health facility.

c) There is continued loss of weight.

Refer children with suspected treatment failure for further assessment.

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.

4.3.7 Ways to Improve Adherence

- Explain and emphasize to care-givers and children why they must take the full course of treatment even if they are feeling better.
- Note risk factors for poor adherence and address them accordingly. These include distance/ transport; being an orphan (especially if the mother has died) or primary care-giver is unwell; and adolescents.
- Ensure education and adherence support especially for TB/HIV co-infected patients.

Treatment Interruptions

To be managed as per the treatment interruptions guidelines in the adult TB chapter 3.

4.3.8 Adverse Drug Reactions of Anti TB Drugs in Children

Adverse events caused by anti-TB drugs are much less common in children than in adults. Anti-TB drugs in children are generally well-tolerated and safe. Side effects occur and are managed *similar to the adults; refer to chapter for the management of common ADRs.*

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 for **all children** on TB treatment or Isoniazid.

4.4 DR TB in Children

Diagnosis of DR-TB in children

In children, DR-TB is mainly the result of the transmission of DR-TB bacilli from an infected adult source. It should be highly suspected in a child with a history of exposure to a known DR-TB case or a person with a chronic cough.

DR-TB should be suspected when:

1. There is contact with known DR-TB
2. There is contact with suspected DR-TB, i.e. source case had treatment failure or was previously treated
3. A child with TB is not responding to first-line therapy despite adherence
4. 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). Rapid DST of Isoniazid and Rifampicin or Rifampicin alone is recommended over conventional testing or no testing at the time of diagnosis. Children without bacteriological confirmation but are highly suspected to have drug-resistant TB should be initiated on DR TB treatment.

4.4.1 Treatment of DR-TB in Children

Treatment of DR-TB in children should be guided by the DST results. In children for whom DST results are not available, the DST pattern may be assumed to be similar to that of the contact.

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. These children should be offered empirical treatment based on the contact`s DST pattern.

Drugs used for the treatment of children with MDR-TB

- The regimen used to treat childhood drug-resistant TB may be different from that used in adults. Pediatric friendly formulations are recommended where available.
- The benefit of fluoroquinolones far outweighs the risk and should be part of every DR-TB regimen.
- Bedaquiline is recommended for use in children above 6 years of age. Bedaquiline can be dissolved in water without altering the bioavailability; which makes it easier for use in young children until the paediatric friendly formulation becomes available.
- Delamanid is recommended for use above 3 years of age but it could be considered in children <3 years once safety and dosing data is available. There is no current recommendation for its routine use in this age group. Delamanid should not be crushed or dissolved as this will alter the drug's bioavailability.
- Both bedaquiline and delamanid should be used for six months of treatment, though there are no known safety concerns with using these drugs for longer than six months. Some children may benefit from using these drugs for the full duration of their therapy.

There is limited data on the use of bedaquiline and delamanid in combination—although existing data suggest the combination of the two medications does not increase adverse events. In children with fluoroquinolone resistance or in whom there are limited treatment options, extension and combination of bedaquiline and/or delamanid could be considered on a patient-by-patient basis with careful monitoring.

- Empiric treatment for DR-TB should be initiated promptly, using an appropriate regimen based on the resistance pattern of the source case.
- Drug dosages should be based on body weight and the higher end of the recommended range[5].

Recommended regimen for treatment of DR-TB in children

Treatment is provided for 18 months: 6 months of intensive phase and 12 months of the continuation phase

Table 4.13: Recommended regimen for treatment of DR-TB in children

PAEDIATRIC MDR/RR TB (<6 YRS AND < 25KG) STANDARD PAEDIATRIC INJECTABLE FREE REGIMEN)

Use at least 4 New Medicines or with proven susceptibility

- **Intensive phase: 6 Lzd/Mfx/Cfz/Cs**
- **Continuation phase: 12 Mfx/Cfz/Cs**

Note: for children ≥6 years or ≥25kg use adult regimen. Refer to MDR-TB management in section 8

PRE - XDR PAEDIATRICS - Fluoroquinolone Resistance

- **Intensive phase: 6 Bdq**/*Dlm/Lzd/Cfz/Cs/Z**
- **Continuation phase: 14 Dlm/Cfz/Cs/Z**

****Delamanid should only be prescribed in children under 3 years after consultation with the National Clinical team***

*****Bedaquiline use in Paediatrics requires dissolution in water***

BDQ=Bedaquiline, CFZ=Clofazimine, CS=Cycloserine, DLM= Delamanid, LZD=Linezolid, MFX=Moxifloxacin, Z=Pyrazinamide

Follow up of children on DR-TB treatment

- 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 review and follow the progress of **all paediatric cases.**

Refer to chapter 8 for monitoring schedule for patients with DR-TB and for management of common side effects of second-line treatment.

4.5 TB and HIV Co-infection in Children

Most paediatric HIV infection occurs prenatally through vertical transmission. HIV disease progresses rapidly in children with ~50% of them developing severe immune-suppression and dying before 2 years of age if they do not access antiretroviral therapy. In this setting, when these children are infected with TB, TB progresses even more rapidly to severe disease with high mortality. These children are at high risk of TB infection as they live in households where a parent is also likely to have HIV disease and have a higher probability of developing active TB. Similarly, TB co-infection itself causes a more rapid progression of HIV disease.

HIV-infected children may have multiple and concurrent opportunistic lung infections that clinically present like TB, thus making the diagnosis of TB in an HIV-infected child more difficult. The ARVs and anti-TB drugs have potentially significant drug-drug interactions as well as overlapping toxicities that pose additional challenges in treating co-infections. Therefore, a comprehensive approach to the management of both TB and HIV is critical.

4.5.1 Diagnosis of TB in HIV

The approach to diagnosis of TB in HIV-infected children is similar to HIV uninfected children. History of contact with TB is extremely important in pointing to the possibility of TB disease in a younger, HIV infected child.

Symptom-based TB screening using the Intensified Case Finding tool *(Refer to appropriate SOP)* MUST be performed for all children living with HIV at every clinic visit to rule out active TB; patients who screen positive (presumptive TB cases) must be evaluated according to the algorithm for TB diagnosis. Patients who screen negative should be initiated on Isoniazid Preventive Therapy (IPT) according to the guidelines.

Together with TB symptoms, a positive Mantoux test is suggestive of TB disease. A positive Mantoux test without symptoms or features suggestive of TB should not be used to diagnose TB in children (see algorithm for TB diagnosis in children). Any child with a positive Xpert MTB/RIF test result should be started on anti TB treatment. **A negative Xpert MTB/RIF test result however doesn't indicate the child has no TB; further clinical evaluation is needed to make a clinical diagnosis of TB in such children.**

4.5.2 Diagnosis of HIV in TB

HIV testing should be voluntary and conducted ethically in an environment where the five Cs - Consent, Confidentiality, Counseling, Correct results, and Connection (linkage) - can be assured.

For all children and adolescents with TB under the age of 15 years, conduct HIV testing and counselling (with parental consent). Adolescents 15 years and above can give consent for HIV testing and counselling. Infants should be tested according to the available guidelines for HIV diagnosis in infants aged <18 months. A positive HIV antibody test in a child younger than 18 months of age confirms HIV exposure.

All HIV Exposed Infants (HEI) should be tested with DNA PCR within 6 weeks of age or 1st contact thereafter, and if negative then another DNA PCR at 6 months, and if negative then another DNA PCR at 12 months. This replaces previous guidelines to perform antibody testing for infants at 9 months.

An antibody test should be performed for all HEI at 18 months, and 6 weeks after complete cessation of breastfeeding.

4.5.3 Differential Diagnosis in HIV Infected Child with Chronic Respiratory symptoms

The diagnosis of PTB can be particularly challenging in an HIV-infected child because of clinical and radiological overlap with other HIV-related lung diseases. The respiratory system is a common site for many opportunistic infections in HIV infected children. Often there is co-infection as well, which further complicates the diagnosis, other possible causes of chronic lung disease in HIV infected children are shown in the table below:

Table 4.14: 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	A common cause of acute severe pneumonia, severe hypoxia especially in infants. CXR: diffuse interstitial infiltration and hyperinflation
Tuberculosis	Persistent respiratory symptoms not responding to antibiotics. Often poor nutritional status. Positive TB contact especially in younger children CXR: focal abnormalities and perihilar adenopathy

Differential Diagnosis	Clinical features
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 Characteristic lesions on skin or palate

4.5.4 Treatment of TB in HIV in Children

All Children and adolescents living with HIV (CALHIV) qualify for ART irrespective of WHO Clinical Stage, CD4 count, age, gender, pregnancy status or co-infection status, etc. Any child with active tuberculosis should begin TB treatment immediately, and begin ART as soon as the TB treatment is tolerated; i.e. no nausea or vomiting and no on-going or evolving adverse drug events, usually 2 to 8 weeks of TB therapy.

Once a diagnosis of TB is made in an HIV infected child, TB treatment should be initiated as a matter of urgency, regardless of whether the child is on ART or not.

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. However, response to TB treatment may be slow in children living with HIV.

All children with TB/HIV should receive Cotrimoxazole prophylaxis as well as antiretroviral therapy. Nutritional support is often needed for children with TB/HIV.

Recommended ART Regimen for TB HIV Co-infection in Children Living with HIV (CALHIV)

The preferred ART Regimens for children with TB/HIV Co-infection are as shown in the Table 4.15:

Table 4.15: Recommended ART Regimen for TB HIV Co-infection in Children Living with HIV (CALHIV)

Age	Scenario	Recommendation
<20kgs[a]	ABC/3TC/LPV/r	Super Boost LPV/r[c]
20kgs-35kgs	ABC/3TC/DTG	RAL at x2 standard weight-based BD dosing until 2 weeks after completion of Anti-TBs
>35kg	TDF/3TC/DTG	DTG[b] x2 standard dose BD dosing
a. For children who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is RAL (double-dose) if ≥ 2 years old, if < 2 years old use a triple-NRTI regimen of ABC + 3TC + AZT for the duration of TB treatment, **then return to ABC + 3TC + LPV/r upon completion of TB.** b. For children >35kgs HIV-TB co-infected to use DTG x2 standard dose BD dosing. Those who cannot tolerate DTG, the alternative is RAL at X2 standard weight-based BD dosing c. For patients on these regimens who become viremic consult Regional or National HIV Clinical Support Center (ulizanascop@gmail.com) or call Uliza Toll-free Hotline 0800 72 48 48		

3TC=Lamivudine, ABC=Abacavir, AZT=Zidovudine, DTG=Dolutegravir, LPV/r=Lopinavir/ritonavir, RTV=Ritonavir, TDF=Tenofovir

Always weigh the child and adjust the TB and ARV dosing accordingly

Refer to national guidelines on Anti-retroviral therapy for Paediatric ARV dosing

Triple nucleoside ART should NOT be used in TB/HIV co-infected patients who have previously failed ART

4.5.5 Cotrimoxazole Preventive Therapy (CPT)

Cotrimoxazole has been shown to reduce mortality among children infected with HIV. All TB/HIV co-infected children should be offered CPT and it should be started as soon as possible. The duration of treatment is usually life-long with once-daily dosing.

The children should be monitored for side effects, which include skin rashes and gastrointestinal disturbances. Severe adverse reactions are uncommon and usually include extensive exfoliative rash, Steven-Johnson syndrome, or severe anemia/pancytopenia. CPT should be discontinued if a child develops severe adverse reactions. The recommended dosage of Cotrimoxazole for children is shown below.

Table 4.16: Recommended dosages for Cotrimoxazole Preventive Therapy

Weight in Kg	Child Suspension (200mg/40mg per 5ml)	Child Tablet (100mg/20mg)	Single strength adult tablet (400mg/80mg)	Double strength adult tablet (800mg/160mg)
<5	2.5ml	One tablet	¼ tablet	-
5-15	5ml	Two tablets	½ tablet	-
15-30	10ml	Four tablets	One tablet	½ tablet
>30	-	-	Two tablets	One tablet

When Dapsone (as a substitute for CPT) is being used as PCP prophylaxis, it is only recommended for patients in WHO stage 4. It is given at **2mg / kg once daily (maximum dose 100mg).** It is supplied in 25mg and 50mg tablets

4.5.6 Immune Reconstitution Inflammatory Syndrome (IRIS)

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

IRIS is managed by continuing anti-TB therapy and giving non-steroidal anti-inflammatory drugs until severe symptoms subside. *Refer to the National HIV Guidelines for the management of IRIS.*

Prednisone is given at 2mg/kg once daily for 4 weeks, and then taper down over 2 weeks (1mg/kg for 7days, then 0.5mg/kg for 7 days then stop).

4.5.7 Prevention of TB in HIV Infected Children

All HIV-infected children need to be screened for TB. 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 TB preventive therapy according to the LTBI guidelines in section 11. In children living with HIV who are less than 12 months of age, only those who have contact with a TB case, and who are evaluated for TB should receive TB preventive therapy (TPT) if the evaluation shows no TB disease.

Deliberate efforts should 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. Always examine the placenta for tubercles because their presence may implicate vertical TB transmission.

BCG vaccine is to be given to all newborn babies except those with symptoms of severe HIV infection. It is also not given to children who started TPT before its administration. In these children, complete the TPT course and wait 2 weeks after TPT completion to give BCG.

4.6 Prevention of TB in children

4.6.1 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 child is malnourished children
- The child is under 5 years
- The child is HIV infected.

Disease usually develops within 2 years of infection. In infants, the time lag can be as short as a few weeks. TB preventive therapy for children exposed to TB who have not yet developed disease will greatly reduce the likelihood of developing TB.

Contact screening refers to the evaluation for TB of all children who are close contacts of bacteriologically confirmed PTB cases

Reverse contact screening refers to the evaluation of all possible source cases of a child diagnosed with TB disease.

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 TB Preventive Therapy (TPT) for the high-risk children who have no signs or symptoms of TB disease.

4.6.1.1 Process of Contact Investigation (CI)

When CI is initiated the index case should be interviewed as soon as possible after the diagnosis (generally within one week) to elicit the names of household members and other close contacts. The focus should be on household members, where the yield is potentially highest, but workplace and social contacts should not be ignored.

If the human resources are available, the person conducting the CI should visit the home of the index patient to ensure that all contacts are interviewed and referred for evaluation when indicated. This is usually done by the community volunteer or at times the health care worker. The visit will give a more accurate view of the actual circumstances of the exposure and provide an opportunity for identification of needed social support, and for education regarding tuberculosis and infection control measures that may be taken.

If a child presents with active tuberculosis, it is important to conduct what is often referred to as "reverse contact tracing." Most sick children contracted tuberculosis from an adult with the disease with whom they have had close contact. With reverse contact tracing, attempts are made to identify the adult who is the source of the infection.

Data on CI should be collected in the recommended contact tracing tools availed by the National TB program.

Contact screening is done using a symptom screen using the set of questions as listed in the ICF tool. These include:

1. Cough
2. Fever and/or night sweats
3. Weight loss or Poor weight gain (Failure to thrive)
4. Lethargy/reduced play/less active
5. Extrapulmonary signs and symptoms e.g. enlarged cervical LN.

A child or contact that has any of the signs and symptoms of TB should be referred to the nearest health facility to have a full evaluation for TB.

Contacts found to have TB disease are initiated on the full course of treatment while those without TB are counselled to identify signs and symptoms and advised when to return. All child contacts are initiated on TPT once TB disease has been ruled out.

4.6.2 TB Preventive Therapy (TPT) in Children

TPT should be given to the following categories of children:

1. Children < 5 years of age who are contacts of bacteriologically confirmed TB patients
2. Children over 5 years' who are household contacts of a person with bacteriologically confirmed TB patients
3. All HIV positive children above one year.

4. Children below one year living with HIV and are household contacts of bacteriologically confirmed TB patient

Refer to LTBI section 11 for diagnosis, testing, and management of latent TB infection

Important to Note:

- Follow up of a child on TPT is done monthly. If TB disease develops in the course of TPT management, stop TPT, and treat for TB.
- All children on TPT should receive pyridoxine
- **TPT 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**

4.6.3 BCG Vaccination

BCG is a live attenuated vaccine derived from *Mycobacterium bovis*. It offers protection against the more severe types of TB such as Milliary TB and TB meningitis, which are common in young children.

A child who has not had routine neonatal BCG immunization and has symptoms of advanced HIV disease (WHO stage 3 or 4) should not be given BCG because of the risk of disseminated BCG disease. In children with suspected TB infection or disease, the BCG vaccination should be deferred till 2 weeks after completion of TPT/TB treatment because the anti-TB medicines will denature the vaccine.

4.6.3.1 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 an 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 immunodeficiency and treated for TB using the first-line regimen: 2RHZE then 4RH. The child should always be reviewed by a specialist.

4.7 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. The national figure for acute malnutrition of children under five years old is estimated at 6%.

Children can have a combination of both acute and chronic. Acute malnutrition is categorized into Moderate Acute Malnutrition (MAM) and Severe Acute Malnutrition (SAM), determined by the patient's degree of wasting. All cases of bi-lateral oedema are categorized as SAM.

Chronic malnutrition is determined by a patient's degree of stunting, i.e. when a child has not reached his or her expected height for a given age. To treat a patient with chronic malnutrition requires a long-term focus that considers household food security in the long run; home care practices (feeding and hygiene practices); and issues related to public health.

SAM is further classified into two categories: Marasmus and Kwashiorkor. Patients may present with a combination of the two known as Marasmic-Kwashiorkor. Patients diagnosed with Marasmic-Kwashiorkor are extremely malnourished and at great risk of death.

Admission criteria for acute malnutrition are determined by a child's weight and height, by calculating weight-for-height as a "z-score" (using WHO Child Growth Standard, 2006), and the presence of oedema. All patients with bilateral oedema are considered to have severe acute malnutrition. See table 4.17 for anthropometric criteria.

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, height, and MUAC. The MUAC will be an indicator of acute malnutrition and if recent will call for the appropriate interventions. The weight is then assessed at every visit and appropriate drug adjustments are made in case of weight gain.

For children 0-59 months of age their age, weight, and height/length is taken and Z–Scores are recorded as per the reference charts. For children 5-19 years, their age, weight, and height are used to assess the BMI for age.

4.7.1 Nutritional Assessment, Counselling and Support (NACS) process

All children diagnosed with TB should receive a nutritional assessment, counselling, and support, tailored to the individual needs of the patients, including:

- Nutrition assessment and diagnosis
  - Anthropometric
  - Biochemical investigations
  - Physical and clinical examination

- Dietary (24 hr recall for food type/frequency and household food security)
- Environmental and psychosocial
- Functional (ability to care for self, bedridden, etc.)

• Counselling& education
  - Benefits of maintaining good nutritional status to a TB patient
  - On infant and child nutrition (ICN)
  - Identifying locally available foods they can access given their context, food safety, and food preparation
  - Helping the client to plan meals and snacks with a variety of foods to meet their energy, high protein, and nutrient needs and treatment plans
  - Identifying any constraints the client may face and find ways to minimize them
  - Helping the client to understand the potential side effects and food interactions of the medicines they are taking, and help the client identify ways to manage these side effects
  - Exploring with the client the cause(s) of poor appetite and appropriate responses (type of food, disease, pain, depression, anxiety, or side effects of medications)
  - Counseling on high levels of sanitation and food hygiene

• Support
  - Nutrition care plan
  - Therapeutic and supplementary foods (food by prescription, therapeutic feeds, fortified blended flour)
  - Complementary foods for children ≥6 months
  - Micronutrient supplements
  - Point-of-use water purification to prevent water-borne disease
  - Food security and linkage to community

Upon assessment, anthropometric criteria are used to classify the nutrition status of the child as shown in the Table 4.17:

Table 4.17: 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 -2 to <-1 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
MUAC (6 - 59 months only)	<11.5cm	11.5 to 12.4cm	12.5-13.4cm
Oedema	Oedema Present	Oedema Absent	Oedema Absent
Adolescent (10 years to 18 years)			
MUAC	< 16cm	N/A	N/A
Oedema	Oedema Present	Oedema Absent	Oedema Absent

Anthropometric criteria based on WHO Child Growth Standards (2006) Mid-Upper Arm Circumference (MUAC) is often the screening tool used to determine malnutrition for children in the community under five years old. A very low MUAC (<11.5cm for children under five years) is considered a high mortality risk and is criteria for admission with severe acute malnutrition. Table 4.18 outlines MUAC criteria for children under-five years.

Table 4.18: MUAC criteria to identify malnutrition of children less than 5 years in the community

Severely Malnourished	Moderately Malnourished	At-Risk of malnutrition
Less than 11.5cm	11.5cm to 12.4cm	12.5cm to 13.4cm

Classifying nutrition status using weight for age

In selected situations, one may not be able to get an accurate height. This may happen in:

- Children who are very sick, disabled, have neurologic abnormalities, or very irritable
- Instances where the instruments to measure height are not available

In such circumstances, one may use weight for age assessment in children up to 14 years. Use the weight for age WHO charts to assess the nutrition status of the child.

To determine the nutrition intervention to be given to the child, the triage criteria is as shown in the table below:

Table 4.19: Triage to determine treatment of malnutrition

ASK:	Has there been any weight loss in the previous month? Does the patient have an appetite? Does the patient have any medical condition that will impair nutritional status? Is the breast-feeding child suckling well?
LOOK AND FEEL FOR:	Visible signs of wasting
CHECK:	MUAC Weight Height/length Bilateral-edema
DETERMINE:	Level of malnutrition using W/H reference charts (or W/A)
LOOK AT SHAPE OF GROWTH CURVE:	Has the child lost weight? Is the growth curve flattening?

4.7.2 Nutrition Care Process

Once nutrition assessment has been done and a diagnosis made, the child then needs to have interventions to address their specific nutrition needs. These interventions include nutrition counselling, food supplementation, and food by prescription as summarized in table 4.19 below:

Table 4.20: Steps in the nutrition care process

Nutrition care process	Classification of undernutrition	
	Severe	**Moderate / mild**
Nutrition Assessment	1. Look for signs of severe wasting • loss of muscle mass • severe visible wasting 2. Check for the presence of bilateral pitting edema • any grade 3. Measure the MUAC 4. Take weight 5. Check for medical complications 6. Conduct an appetite test	1. Take weight 2. Measure the MUAC 3. Assess dietary intake 4. Check for medical complications 5. Assess the social economic status 6. Check for bilateral pitting oedema 7. Check for clinical signs of malnutrition

Nutrition care process	Classification of undernutrition	
	Severe	Moderate / mild
Nutrition Diagnosis	• Signs of severe visible wasting • Bilateral pitting Oedema (+, ++, +++)	
Nutrition intervention	• Nutrition and infant feeding counselling • Provide 200 Kcal/Kg/day RUTF 279gms per day of RUTF i.e., (21 sachets per wk) • 200- 300 grams per day FBF every 2 weeks or monthly • One bottle (150 ml) of SWS*per month • Inpatient stabilization care to treat underlying illnesses	• Nutrition and infant feeding counselling • Provide 200- 300 grams per day of FBF (for mild malnutrition) • Provide 200 Kcal/Kg/day RUTF 279gms per day of RUTF i.e., (21 sachets per wk for moderate malnutrition) • One bottle (150 ml) SWS* per month • Routine basic treatment e.g. Vitamin A, deworming, iron-folic supplementation.
Nutrition monitoring and evaluation	• Check weight weekly • Conduct appetite test weekly • Carry out other nutrition assessments • Give education and counselling as required. • Little or no edema for 10 days and passed appetite test-continue on FBF	• Check weight monthly and height every three months • Carry out nutrition assessment monthly • Give education and counselling as required

4.8 TB in Special Circumstances in Childhood

4.8.1 Management of a Baby Born to a Mother with PTB

Congenital TB is TB acquired in-utero through haematogenous spread via the umbilical vessels, or at the time of delivery through aspiration or ingestion of infected amniotic fluid or cervicovaginal secretions. Congenital TB usually presents in the first 3 weeks of life and mortality is high.

Neonatal TB is TB acquired after birth through exposure to an infectious case of TB - usually the mother but sometimes another close contact. It is often difficult to distinguish between congenital and neonatal TB but management is the same for both. Transmission of TB within newborn units, paediatric wards, and maternity wards does occur in overcrowded health facilities, hence the need to implement infection prevention control measures (including the use of surgical masks) whenever one case of TB has been identified within this setup. This is to reduce transmission to newborns who are extremely vulnerable to TB.

The TB-exposed neonate is highly vulnerable and may rapidly progress to symptomatic and severe TB disease. Symptoms and clinical signs of neonatal TB are usually nonspecific and examples are shown in the table below:

Table 4.21: Signs and Symptoms of Neonatal TB

Symptoms	Clinical signs
Lethargy	Respiratory distress
Fever	Non-resolving 'pneumonia' or respiratory infection
Poor feeding	Hepatosplenomegaly
Low birth weight	Lymphadenopathy
Poor weight gain	Abdominal distension
	Clinical picture of 'neonatal sepsis'

The diagnosis of TB should be included in the differential diagnosis of a child with neonatal sepsis, poor response to antimicrobial therapy, congenital infections, and atypical pneumonia. The most important clue to the diagnosis of neonatal TB is a maternal history of TB or any contact with a person with a chronic cough.

Clinical evaluation of the infant in the setting of suspected congenital TB should include TST and interferon-gamma release assay (IGRA), HIV testing, chest radiograph, lumbar puncture, cultures (blood and respiratory specimens), and evaluation of the placenta with histologic examination (including acid-fast bacilli [AFB] staining culture). The TST in newborns is usually negative, but an IGRA test may be positive in some cases.

4.8.2 Management of the Asymptomatic Neonate Exposed to Maternal TB

If a neonate is born to a mother with TB or is exposed to a close contact with TB, TB Preventive Therapy (TPT) should be given for 6 months once TB disease has been ruled out. BCG can be given 2 weeks after completion of TPT. It is not necessary to separate the neonate from the mother. However, the mother should be educated on infection prevention control measures.

Breastfeeding is not contraindicated for a child whose mother has TB

Neonates born to mothers with MDR-TB or XDR-TB should however be referred for TB screening and management. **TPT should not be given.** Infection control measures such as the mother wearing a mask are required to reduce the likelihood of mother to child transmission of DR TB.

4.8.3 Management of the Neonate with TB Disease

If a neonate who is exposed to a mother or another contact with TB is found to have symptoms suggestive of TB, treatment with anti-TBs should be initiated even while awaiting bacteriological confirmation as TB progresses rapidly in neonates. Drug dosages must be tailor-made based on the neonate's weight. Breastfeeding is encouraged.

4.8.4 TB Among Children in Congregate Settings

Children may contract TB in congregate settings outside the household. These congregate settings include childcare (daycare) centers, orphanages, prisons (juvenile prisons), (day and boarding), and refugee camps. This is due to several factors including overcrowding, poor hand hygiene, poor cough etiquette, poor ventilation, and general poor TB infection control measures in place.

Once a child has been diagnosed with TB within the congregate setup, all efforts must be made to screen all contacts of the diagnosed child, while conducting reverse contact tracing to identify the index case. All presumptive TB cases must be evaluated according to the algorithm for TB diagnosis and those diagnosed with TB initiated on treatment. Where feasible, older children with bacteriologically confirmed TB within these congregate settings should be separated or isolated from others until they are considered at low risk for transmission (after sputum conversion).

Congregate settings are an important component of the country's TB surveillance activities and should be assessed for TB infection control. Such assessments should be followed by the screening of all presumptive TB cases and development of infection prevention and control plans to support administrative, environmental, and respiratory measures.

LABORATORY DIAGNOSIS OF TB

5

5.1 Introduction

Identification of MTBC and the subsequent isolation of resistant strains is key in Tuberculosis (TB) management. Tuberculosis (TB) diagnostic laboratories play a critical part by providing clinicians with invaluable confirmation of diagnosis, guiding the care of patients and follow up of those with confirmed pulmonary disease. The networking of laboratories offering TB diagnostics requires a tiered network of laboratories diagnostic tools and establishment of sample referral mechanisms which is crucial in increasing access. All this should be tied up with quality assurance for effective laboratory management. There are a number of currently available WHO-recommended diagnostic techniques for detection of drug susceptible TB and drug resistant TB that are suitable for complimentary use at the different levels of the tiered network of TB laboratories. Among TB patients on treatment with poor response (clinical and bacteriologic i.e. smear and/or culture conversion), DST is required for identification of possible resistance. Smear microscopy is key for follow-up of patients with confirmed pulmonary DS TB. In patient with DR TB, monthly smear microscopy and culture are mandatory during follow up.

KEY HIGHLIGHTS:

- **GeneXpert MTB/RIF Assay/ Xpert MTB/RIF Ultra is the initial test for TB diagnosis in Kenya while microscopy should be used for follow up smears.**
- **Stool sample can be used for pediatric MTB diagnosis using GeneXpert MTB/RIF Assay/ Xpert MTB/RIF Ultra.**
- **Interferon Gamma Release Assay (IGRA) may be used for diagnosis of latent TB infection.**
- **TB LAM is a complementary test for TB diagnosis in PLHIV.**

5.2 Laboratory Diagnosis of TB

Laboratory methods for identification of TB and anti-microbial resistance are broadly classified into:

a) Microscopy

- Light-emitting diode (LED) fluorescent microscopy
- Conventional light microscopy

b) Molecular and new technologies

- Xpert MTB/RIF assay
- Xpert MTB/RIF ultra
- Line Probe Assay
    - 1st and 2nd line
    - Identification of MOTTs/NTMs
- Sequencing
- BD Max- MDR -TB
- Truenat.

c) Phenotypic culture for detection and identification of TB

Commercial liquid culture systems

Culture on solid media

d) Drug susceptibility testing

DST first line-anti TB-agents

DST second-line anti-TB agents

e) Rapid identification tests

- TB LAM Urine test for PLHIV

f) Immuno diagnostic tests used for Latent TB

- Interferon Gamma Release Assay (IGRA)

Both the DNTLD Program and the National TB Reference Laboratory (NTRL) coordinate diagnostic services, while the National laboratory technical working group (TWG) guides in implementation of TB laboratory services.

In the Public sector NTRL and KEMRI CDC Kisian carry out both culture and DST and additional facilities i.e. Malindi Sub County Hospital, Kitale County Referral and Machakos Level V Hospital have been established to carry out molecular testing for TB. All these facilities are supervised by NTRL for purposes of maintaining quality.

5.3 Specimen Collection

Sample types

Table 5.1: Types of Specimen for every test method and the Handling Procedures

Test	Specimen Type	Type of container	Specimen volume	Transport /storage conditions
Microscopy	Sputum, CSF, Aspirates, Biopsies, Pus/ swabs	A wide-mouthed, unbreakable, leak-proof container	3-5ml	2 – 8°C
MTB Rif Assay (Gene Xpert)	Sputum, CSF, Gastric aspirate, Nasopharyngeal aspirate, Pleural fluid, Pericardial fluid, Ascitic fluid, FNA, Lymph node biopsy, Stool, skin snips, pus aspirate, bone tissue.	50 ml falcon tubes	2-3ml	2 – 8°C
TB culture / DST	Sputum, CSF, Aspirates, Biopsies, pleural effusions, urine, Laryngeal swab, gastric aspirates, pus swabs	50ml falcon tubes, 28ml sterile universal bottles	Bronchial secretion (2–5ml), BAL (20–40 ml) Pleural effusions (20–50 ml) CSF-(3ml) Urine(200ml)	2 – 8°C
IGRA (QuantiFERON) Assay	Blood	Whole blood collected in EDTA tubes	4-6mls	2 – 8°C
LPA	Sputum, CSF, Aspirates, Biopsies, pleural effusions, laryngeal swabs, gastric aspirate pus swabs	50ml falcon tubes 28ml sterile universal bottles	Bronchial secretion (2–5ml), BAL (20–40 ml) Pleural effusions (20–50 ml) CSF-(3ml) Urine (200ml)	2 – 8°C

NOTE:
Sample Referral to the Decentralized LPA Labs

- Two samples will be collected from the patient
- One sample will be tested in the decentralized lab for 1st and 2nd line LPA-DST
- The second sample will be sent for phenotypic DST to the reference lab

NB: The second sample should be sent by the LPA lab for accountability and follow up of the report.

Types of samples

1. Sputum

For good quality specimens to be obtained, patients must be instructed on how to produce sputum ***(Refer to sputum collection job aid).*** Label each specimen with the patient's name as it appears on the laboratory request form ***(Refer to laboratory request form).***

Sputum collection procedure

NOTE:
- The best specimen comes from the lungs.
- Saliva or nasal secretions are unsatisfactory.
- Specimens should not contain food or other particles because the test may not work properly.

Instructing patients to collect sputum specimen

Patients should be instructed to take the following steps to produce the best specimen:

1. Sputum collection/expectoration should be done in an open space/Cough corner/sputum collection booth
2. Wash your mouth with clean water to remove food and other particles
3. Inhale deeply 2–3 times and breathe out strongly each time
4. Cough deeply from your chest to produce sputum
5. Place the opened container close to your mouth to collect the specimen; do not get sputum on the outside of the container
6. Close the container tightly
7. Submit to the laboratory as soon as possible.
8. Do not use the request form to wrap the specimen
9. Wash your hands after collecting the sample.

Instructions for HCWs who collect patient samples for evaluation

1. Fill in the sputum examination forms ensuring that all the fields are correctly filled.
2. Instruct the patient to collect sputum samples in a well ventilated area or a designated cough corner preferably outdoors (not in the facility lavatories).
3. Label the sputum containers on the side (not on the lid) after sputum collection.
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.

2. 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 a few drops of sterile 0.9% saline to the tissue.

NOTE:

Specimens are sometimes sent in formalin. It may therefore be advisable to remind the physician of the expected collection conditions, the day before surgery.

- **Gastric Aspirate**

Gastric aspirates often contain MOTT and are therefore rarely used for adults; they are indicated for children, however, who are not likely to produce sputum.

An early morning specimen is highly recommended especially when the patient has an empty stomach.

After specimen collection, add 100 mg of sodium bicarbonate to the gastric aspirate to neutralize it and transport immediately to the laboratory or store at 2-8 °C ***(Refer to PMDT Guideline)***.

3 Other Extra-pulmonary specimen

The laboratory may receive a variety of specimens for diagnosis of extra-pulmonary TB – body fluids, tissues, urine etc. All these samples should be sent for GeneXpert, and culture and DST. 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.

- All liquid specimens should be collected in sterile glass containers without using any preservative.
- Specimens can be inoculated directly into liquid vials and transported to the laboratory for culture.
- Specimens must be transported to the laboratory immediately; they should be processed as soon as possible or kept at 2–8 °C.

Specimens collected from non-sterile sites

- A urine specimen should consist of a single, early-morning, midstream sample.
- Skin tissues, pus swabs and pus aspirates
- Stool samples from children for GeneXpert from immunocompromised patients may be used mainly to detect MOTT (Microscopy and Culture).

NOTE:

All extrapulmonary samples should be considered for culture and DST.

5.4 Laboratory Request form

The laboratory request form must be clearly and completely filled with all the necessary patient details ***(Reference Sample request form)***.

NOTE: Additions in the request form

- Index case details
- DR TB contacts
- Referral lab
- Person referring the sample
- Stool as a sample for paediatric TB testing

5.5 Transport and Packaging

The basic packaging system for local surface transport of all specimens consists of triple packaging systems while ensuring that the Biohazard labels are attached on the outer shipping package as per IATA regulations.

Basic triple packaging system consists of three layers as follows;

1. Primary receptacle. A labelled primary watertight, leak-proof receptacle containing the specimen. The receptacle is wrapped in enough absorbent material to absorb all fluid in case of breakage.
2. Secondary receptacle. A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.

Outer shipping package. The secondary receptacle is placed in an outer shipping package which protects it and its contents from outside influences such as physical damage and water while in transit.

NOTE:

All samples should be transported in cold chain (cool box, ice packs and if possible with thermometers to monitor the temperature from packaging to reception of the sample).

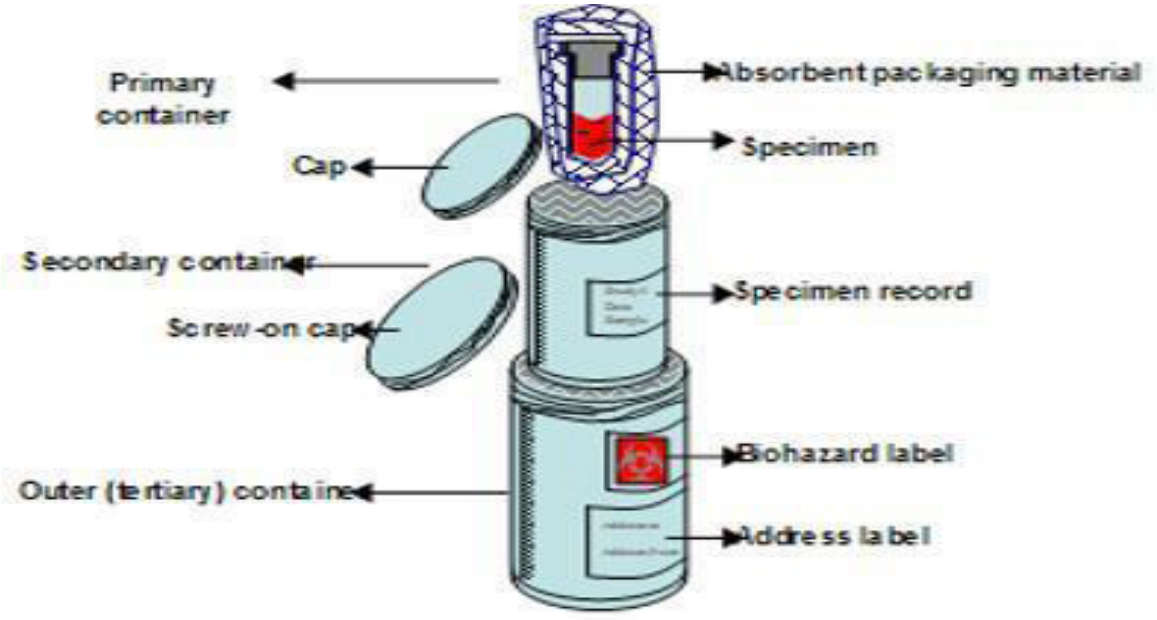


Figure 1: Packing and shipping infectious materials

a) 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 2-8˚c) 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.

b) Sample Acceptance/ Rejection Criteria

Quality specimen is a key to quality results hence, **samples should be accepted when;**

- Collected in a leak proof container
- The volume is adequate (3-5ml)
- Duly completed request form
- Specimen packed appropriately (triple packaging)
- Accurately labelled for identification (Patient's name, IP/OP/TB No, facility name, date).

Samples are rejected when;

- The request form is not received with the specimen or it's not correctly filled.
- There is a mismatch of information details on the request form with details on the specimen container.
- Container used is not appropriate
- Specimen unlabelled.
- Specimen container is broken.
- Specimen leaked.
- Specimen volume is not sufficient.
- Specimen not appropriately packed (triple packaging).

NOTE:

- **Contact the clinician or relevant person before rejecting any sample.**
- **Rejected samples and request forms should still be assigned a laboratory number for record purposes.**
- **The reason for sample rejection should be indicated on the request form and in the register, then dispatched and notification done to the referring facility.**

5.6 Laboratory Testing

5.6.1 GeneXpert (Xpert MTB/RIF Assay/ Xpert MTB/RIF Ultra)

The development of the Xpert MTB/RIF assay (Cepheid USA) was a major step forward for improving the diagnosis of TB and detection of rifampicin resistance globally (WHO). GeneXpert is the recommended initial test for TB diagnosis and the detection of rifampicin resistant TB in Kenya. The Xpert® MTB/RIF assay is a cartridge-based, automated diagnostic test that can simultaneously identify Mycobacterium tuberculosis complex bacteria (MTBC) and resistance to rifampicin (RIF) in less than two hours, using the GeneXpert® platform with high degree of specificity. However, the Xpert MTB/RIF sensitivity is suboptimal, particularly in smear-negative and HIV-associated TB patients. The Xpert MTB/RIF Ultra was developed by Cepheid as the next-generation assay to overcome these limitations. It uses the same GeneXpert® as the Xpert MTB/RIF.

Patients diagnosed with TB using the GeneXpert platform 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. ***(Refer to TB screening and diagnostic Algorithm).***

Table 5.2: the strengths and limitations of GeneXpert (Xpert MTB/RIF Assay) and GeneXpert MTB/RIF ULTRA Assay

Strengths	Limitations
• High sensitivity • Identifies rifampicin resistance • Reliable • TAT shorter compared to culture • TAT is further improved by use of gene Xpert Detection limit of as few as 131 colony forming units/mls of MTB compared with approximately 10,000 colony-forming units/mL with conventional smear microscopy	• Requires a stable electricity supply • The shelf life of the cartridges is only 18 months • The instrument needs to be recalibrated annually • The cost of the test cartridges • Requires temperature monitoring is critical • Requiring centralised laboratories with specialised facilities • Requires skilled personnel

5.6.2 Microscopy

Sputum smear microscopy is the oldest method for diagnosis of pulmonary tuberculosis. Microscopy has low sensitivity and 10,000 bacilli/ml sputum sample. A spot and a morning sputum sample is collected from presumptive PTB cases for TB diagnosis in sites that do not have GeneXpert machines. A second sample should be sent for GeneXpert testing. Patients diagnosed with TB should be followed up with smear microscopy done at the 2nd, 5^{th,} and 6th months. Specimen other than sputum (sots), are collected from presumptive EPTB cases for diagnosis according to the NTLDP guidelines.

Table 5.3: The strengths and limitations of microscopy

Conventional light microscopy	Light emitting diode (LED) Fluorescent Microscopy	
• Ziehl-Neelsen staining technique. • Turnaround time of 24hours. • Has a sensitivity of approximately 55% and a specificity of approximately 99%.	• Auramine staining technique. • Turnaround time of 24hours. • It has a sensitivity of approximately 72% and a specificity of approximately 81%.	
Strengths of microscopy technique	**Limitations of smear microscopy**	
• Short turnaround time (<1 hr) • Low cost • It is widely available	• Low/moderate sensitivity compared to culture or GeneXpert • Does not differentiate live or dead mycobacteria • Does not differentiate mycobacterium species • Requires skilled personnel	

NOTE:

- **Microscopy for follow up of patients should be done at the peripheral laboratories**
- **For individuals with minimal pulmonary involvement and/ or scanty sputum production, induced sputum, gastric lavage or bronchoscopy can increase test sensitivity**
- **Sputum processing, such as liquefaction or concentration by centrifugation, and the use of fluorescence microscopy can also increase the sensitivity of smear microscopy.**

5.6.3 Line Probe Assay

Line Probe Assay (LPA) is a rapid technique based on polymerase chain reaction (PCR) that is used to detect Mycobacterium tuberculosis complex (MTBC) and drug susceptibility to first line and second line drugs.

- First line LPA (FL LPA) (GenoType *MTBDRplus V2*) – provides DST on rifampicin, isoniazid
- First line LPA (FL LPA) (GenoType MTBDR*plus* V2)- DST to Fluoroquinolones and the second line injectable.

It is also useful for speciation of mycobacteria other than tuberculosis (MOTTs) also known as Non-tuberculous mycobacteria (NTMs) (GLI, 2018).

MTB detection Sensitivity 81.5% Specificity 87.5% Rifampicin resistance detection Sensitivity 97.7%, Specificity 91.8%, INH resistance detection Sensitivity 95.4%, Specificity 89%.

Table 5.4: The strengths and limitations of LPA

LPA strengths	Limitations
• LPA produces results in just 24-48 hours, a vast improvement over the 3 months or longer with conventional methods (culture). • It allows quick triage of confirmed rifampicin resistant or MDR-TB patients into either the shorter MDR-TB regimen or the conventional longer regimen. • Hain LPA can be used to diagnose both pulmonary and Extra-pulmonary tuberculosis. • LPA has a high sensitivity of 98% and a specificity of 100% for direct samples • Hain LPA has drug susceptibility testing for both Rifampicin and Isoniazid • Short turnaround time of 5 hours for MDR-TB detection as compared to cultures which takes weeks • Hain LPA can detect mixed infections especially in samples having NTM and MTBC • MTBDRplus can query presence of an Non-tuberculous mycobacteria and also does not show false negative • Tests can be run on less than 2ml specimen volume. • The same extracted DNA may be used for further testing with Hain LPA • GenoType MTBDRsl endorsed by WHO as a rule in test for XDR-TB • GenoType MTBDRplus can track mono-resistance to rifampicin and/or Isoniazid • Genotype MTBDRplus captures infection due to MTB complex and can differentiate the MTBC complex species i.e. *M. africanum, M.bovis subspp bovis, M.bovis subspp caprae, M. Bovis BCG, M.microti, M. canettii, M. pinnipedii* • Hain line probe assay can be used to diagnose Tuberculosis from both direct specimens and culture including contaminated cultures • Hain LPA has full automation allowing high throughput for high volume laboratories • Hain LPA is environmentally friendly as there is no biohazard waste to dispose after running the test • MTBDRplus ver.2.0 has a higher sensitivity for smear – ve samples (Sensitivity of 79.8% for smear negative - *Valerie Crudu et al JCM 2012)*	• It requires adequate and appropriate laboratory infrastructure and equipment (biosafety level II and III laboratory). • It requires adequate and skilled laboratory staff • Cannot be used as a point of care test.

5.6.4 Culture and Drug Susceptibility Testing for TB

a) Phenotypic Culture

Culture is the gold standard for TB diagnosis and can detect as few as 10-100 viable bacteria/ml. We have two types of culture methods.

- Liquid culture - Mycobacterium Growth Indicator Tubes (MGIT)
- Solid culture - Lowenstein-Jensen (LJ).

These are used for the detection and recovery of mycobacteria. All types of clinical specimens, pulmonary as well as extra pulmonary can be processed for primary isolation.

Table 5.5: The strengths and limitations of phenotypic culture

Solid Culture	Liquid Culture
• Longer TAT of up to 60 days • Low risk of Contamination • Manual technique	• Shorter TAT of 42 days • Higher risk of Contamination • Automated technique • +10% more sensitive compared with solid culture
Strengths of culture techniques	**Limitations of culture techniques**
• Requires as few as 10 bacilli/ml to detect TB • Provides a definitive diagnosis of TB • Allows drug susceptibility testing and DR surveillance	• Slow growth of MTB thus delayed turn-around-time • Requires huge infrastructural capacity to set up • Require trained laboratory technicians to perform the procedure.

5.6.5 Drug susceptibility testing

It is a laboratory technique that determines whether or not TB bacteria will grow in the presence of TB drugs. If bacterial growth is observed, it shows resistance, while No growth shows susceptibility to drugs used. The demand for reliable drug-susceptibility testing (**DST**) increases with the expansion of antituberculosis drug-resistance surveillance, and with the need for an appropriate treatment of drug-resistant tuberculosis**.**

Indications

At the very least, the following patients should have DST for first line drugs

- Previously treated patients;
- Persons who develop active TB after exposure to a patient with documented DR-TB;
- Patients who remain smear-positive at month two and five of therapy;

The following groups are targeted for DST for second-line drugs:

- Patients with a DST showing a resistance to at least rifampicin, isoniazid or both rifampicin and isoniazid at baseline
- Patients who remain culture positive on or after Month 3 DR TB.
- Persons who develop active TB after exposure to a patient with documented DR-TB. (MSF medical guideline 2017).

5.6.6 Interferon gamma release assay-IGRA

The Interferon Gamma Release Assay (IGRA) is a blood test used to detect Latent TB infection. It works by measuring the body's immune response to the TB bacteria. It is used to test for Latent TB infection. ***(Refer to IGRAs job Aid).***

Table 5.6: The strengths and limitations of IGRA

Benefits of IGRA	Limitations of IGRA
• Only a single patient visit required. • Ex vivo tests. • No booster effect. • Independent of BCG vaccination.	• Costly. • More laboratory resources required • Complicated process of lymphocyte separation.

5.6.7 TB LAM

TB-LAM is a rapid point-of-care urine dipstick test based that can be performed at the bedside for detection of mycobacterial lipoarabinomannan (LAM) antigen in urine (TB) (WHO, 2018). LAM antigen, is a lipopolysaccharide present in mycobacterial cell walls, released from metabolically active or degenerating bacterial cells and appears to be present only in people with active TB disease ***(Refer to TB LAM Job Aid)***.

Indications of TB LAM

- PLHIV with advanced disease (WHO stage 3 or 4 or CD4 count ≤ 200 cells/ mm^3 or ≤ 25% for children ≤ 5 years old) with presumed TB.
- PLHIV that have any danger signs of severe illness; respiratory rate > 30 breaths per minute, temperature > 39°c, heart rate >120 beats per minute, unable to walk unaided.
- Currently admitted to hospital
- A useful tool for detecting sputum smear negative patients.
- Diagnose both pulmonary and extra pulmonary TB from one convenient urine sample.

NOTE: TB LAM is a bedside test for TB as an additional test for GeneXpert.

5.6.8 Other new molecular methods to be rolled out

a) Truenat MTB

The Truenat MTB, MTB plus and MTB-RIF diagnostic assays (Molbio diagnostic, Goa, India) were developed in India, and may potentially be used as the same health system level as Xpert/MTB/RIF. Of the above-mentioned assays, MTB and MTB plus are used as initial diagnostic tests for TB while MTB-RIF Dx is used as a reflex tests to detect rifampicin resistance for those with positive results of initial Truenat test. The assay use automated, battery-operated devices to extract, amplify and confirm the presence of genomic DNA loci for TB infection diagnosis by use of real-time micro-PCR. Results for the test can available under 1 hours' time. This test is among the new diagnostic tools the country is planning to adopt under the guidance of National diagnostic committee.

b) BD Max ™

c) Genome Sequencer

5.7 Test turnaround time

Table 5.7: Expected turnaround times (TAT) for the various laboratory techniques/ assays.

Test menu	Lab TAT	Comments
AFB Microscopy	24hrs	All specimens (sputum & SOTS)
TB LAM	30 - 40 min	Urine sample
GeneXpert	48hrs	All specimens except blood
TB culture- **Solid culture**	8 weeks 2-8weeks	Culture Negative Culture Positives
TB culture- **Liquid Culture**	6weeks 5-28days	Culture Negative Culture Positives
TB drug susceptibility testing - RHE - PZA	 7-14 days 7- 21 days	 MGIT DST
Molecular DST –FL-LPA **Molecular DST-SL-LPA** **MTB speciation**	7 working days 7 working days 7 working days	Smear Positives All samples All samples
Gene sequencing **(batched)**	2-14 days	All samples

Table 5.8: Interpretation of laboratory results

Method	Expected results	Interpretation	Management/ Recommendation
Microscopy	Positive (0-9), (1+, 2+, 3+)	MTB bacilli seen.	Start Anti TB treatment (2HREZ/4HR) Send another fresh sample for CDST if GXP is not available on site.
	Negative	This shows the TB bacilli has not been seen however it does not rule out the absence of Tuberculosis infection / disease. Note: Correlate with clinical symptomatology and other relevant history. Seek for second senior opinion from SCTLC or CTLC.	A GeneXpert test is indicated. Use XPERT networking hub/courier model.
Gene Xpert	MTB detected, -Rifampicin Resistance not detected (TS)	This shows that the patient has TB that is sensitive to Rifampicin	Collect fresh samples for Culture DST. **Initiate patient on CAT1 (2HREZ/4HR) treatment.**
	MTB detected Rifampicin Resistance detected	This shows that the patient has rifampicin resistance TB	Collect fresh samples for Culture DST1&2 & 2nd Line LPA. **Initiate patient on DR TB (RR / MDR) treatment.**
	MTB detected Rifampicin Resistance indeterminate (TI)	Patient has TB but the bacterial load is very low to determine resistance patterns. Send another sample	Collect fresh samples for the repeat GeneXpert test and treat according to the second GeneXpert results.
	MTB not detected	This shows MTB has not been detected, however it does not rule out absence of Tuberculosis,	Correlate with clinical symptomatology and other relevant history. Seek for second senior opinion from SCTLC or CTLC.
NOTE: For any invalid or error gene Xpert test outcome, collect another sample and repeat test.			
XPERT MTB/ RIF ULTRA	MTB detected trace (TT)	MTB Detected (Trace), RIF Resistance Indeterminate	

NOTE: Trace results interpretation;

1) HIV, Children and EPTB specimen-consider as true positive results for clinical decisions
2) HIV negative with trace call results positive, collect another sample and use the second result for clinical decision (Clinical/Radiological information can also be used)
3) For any repeat test its advisable to collect two specimen (one for GeneXpert Ultra and the other for LPA

Method	Expected results	Interpretation	Management/ Recommendation
FL LPA (MTBDRPlus)	MTBC detected • rpoB & KatG and inhA-mutation detected	The bacteria is resistant to both rifampicin (rpoB) & Isoniazid (KatG and inhA) drugs.	**Rifampicin and Isoniazid (Including high dose isoniazid) should not be used**
	MTBC detected • rpoB & KatG and inhA - Mutation not detected	The bacteria is susceptible to both rifampicin (rpoB) and isoniazid (KatG and inhA) drugs.	**Rifampicin and Isoniazid (Including high dose isoniazid) can be used**
	MTBC detected • rpoB - Mutation detected • KatG and inhA -Mutation not detected	The bacteria is resistant to rifampicin (rpoB), but susceptible to Isoniazid (KatG and inhA)	**Rifampicin should not be used**
	MTBC detected • rpoB- Mutation not detected • KatG and inhA-Mutation detected	The bacteria is susceptible to rifampicin (rpoB), but resistant to Isoniazid (KatG and inhA).	Isoniazid should not be used (refer to the table above for Isoniazid resistance regimen)
	iii. No MTBC detected	MTB complex is absent	Evaluate patient for other conditions
SLLPA (MTBDRsl)	• gyrA/gyrB-Mutation not detected	The bacteria is susceptible to both fluoroquinolones (gyrA/gyrB) Lfx and Mfx respectively	Fluoroquinolones can be used
	• gyrA/gyrB-Mutation detected	The bacteria is resistant to both fluoroquinolones (gyrA/gyrB) Lfx and Mfx respectively	Fluoroquinolones cannot be used (refer to the table above for regimen design)
	• rrs/eis a) Mutation detected b) Mutation not detected	Aminoglycosides(rrs/eis) Capreomycin, Amikacin, Kanamycin, Viomycin) The bacteria are resistant to all or any of the specific drug The bacteria is susceptible to all the drugs	Avoid the use of injectable drugs in general (refer to the table above on regimen design)
Culture (Solid & Liquid)	Growth/Positive	The patient has mycobacteria (MTB or MOTT)	Continue current treatment
	No growth/ Negative	Absence or non-viable mycobacteria(MTB or MOTT)	

Method	Expected results	Interpretation	Management/ Recommendation
First Line DST	Susceptible/Sensitive, (RHZE)	The bacteria is sensitive to all first line drugs	Treat with 1st line anti TB medicines (2HREZ/4HR)
	Resistance to RH	The patient is an MDR TB	Treat as RR / MDR TB
	Resistance to H,Z,E	The patient is poly resistant	Refer to DR TB Treatment guide for regimen composition
	Resistance to R ONLY	The patient is Mono Rifampicin resistant (RR)	Refer to DR TB treatment guide for regimen composition
	Resistance to H ONLY	The patient is Mono isoniazid resistant	Refer DR TB treatment guide for regimen composition
Second line DST	Susceptible/Sensitive Bdq,Dlm,Lzd,-Clz,Cs,Lfx/Mfx,C-m,Amk,Kan,	The bacteria is sensitive to all second line drugs	Refer DR TB treatment guide for regimen composition
	Resistance to Aminoglycosides (Cm, Amk, Kan)	Resistance to any of the Aminoglycosides is a Pre XDR	Refer to DR TB treatment guide and regimen composition
	Resistance to Fluoroquinolones (Lfx,Mfx)	Resistance to any of the Fluoroquinolones is a Pre XDR	Refer to DR TB treatment guide and regimen composition
	Resistance to Fluoroquinolones (Lfx,Mfx) and Aminoglycosides(Cm,Amk,Kan)	Resistance to both fluoroquinolones and Aminoglycosides is an XDR	Refer to DR TB treatment guide and regimen composition
	Resistance to Bdq/ Dlm/Lzd,Clz,Cs	Resistance to specific drugs	

NOTE:

- **Heteroresistant outcome means the patient harbors both drug-susceptible and drug-resistant bacteria.**
- **Indeterminate for a specific drug or group of drugs means that the assay should be repeated before reporting the results. If the same result is obtained upon re-testing, request for another sample.**
- **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.**
- **Children with high clinical suspicion of TB should be treated for TB even if Xpert is negative.**

Table 5.9: Managing Discordant Results

	Test	Discordant pattern/ reports	Explanation	Recommendation
Smear microscopy VS GeneXpert	Smear microscopy	Negative		
	GeneXpert	MTBC detected		
		RS (Rif. Sensitive)	GeneXpert sensitivity and specificity is superior to smear microscopy.	Collect fresh samples for Culture DST. Initiate patient on CAT1 (2HREZ/4HR) treatment.
		RR (Rif. Resistant)	GeneXpert superior sensitivity and specificity to smear microscopy.	Collect fresh samples for Phenotypic Culture and DST 1st and 2nd Line and LPA 1st and 2nd line.
			GeneXpert looks for Mycobacterial DNA in the rpob loci responsible for Rif. Resistance.	Initiate patient on DR TB (RR / MDR) treatment.
		TI (Rif. Resistant Indetermi-nate)	Poor sample quality. Emphasize on good quality samples. Low bacillary load.	Collect fresh samples for the repeat GeneXpert test and treat according to the second GeneXpert results.
		I(Invalid)	Poor sample quality. Emphasize on good quality samples.	Collect fresh sample for GeneXpert test and treat according to the second GeneXpert results
2.GeneXpert vs Smear microscopy (if no GXP on site)	GeneXpert	MTBC not detected	Repeat both tests on fresh samples.	Rare occurrence. Could be a lab error.
	Smear microscopy	Positive		

	Test	Discordant pattern/ reports	Explanation	Recommendation
3.GeneXpert VS Culture and DST	GeneXpert	MTBC Detected, Rif Resistant.	GeneXpert may pick silent mutations in the rpob genome that would be missed by phenotypic testing.	Start on RR/MDR TB treatment regimen. Adjust regimen according to SLLPA results.
				Obtain fresh sample for Genome sequencing.
	Culture and DST	MTBC Pos Rif Sensitive		Continue DR TB treatment.
4. Xpert vs LPA	GeneXpert	RIF resistance detected	The methods look at the same region but detect resistance using slightly different probes. Xpert detects mutations in codons 531,516 and 526 which are not detected by LPA	Start the patient on DR TB treatment.
	LPA	RIF sensitive		
	Xpert	RIF resistance not detected	The methods look at the same region but detect resistance using slightly different probes.	Start the patient on DR TB treatment.
	LPA	RIF resistance detected		
	Xpert	No MTBC detected in a symp-tomatic patient.	Repeat test on a fresh sample. Send another sample for phenotypic testing (CDST) Genome sequencing is recommended.	The second GXP test result to guide the Sub county clinical team's decision.
	LPA	Hetero-resistance detected (HR)		Treat the patient for DR TB.

	Test	Discordant pattern/ reports	Explanation	Recommendation
5.GXP,LPA and Culture discordance	Molecular (Xpert and LPA)	Molecular no MTBC detected	Culture is our gold standard	The sub county clinical team to review the patient and decide on next action based on the patient's condition.
	Culture	Growth reported	Subject the culture isolate to LPA	Treat as per LPA result.
	Molecular (Xpert and LPA)	MTBC detected	Order another sample for phenotypic CDST	Treat as per molecular results.
	Culture	culture negative	Non-viable cells	Continue treatment as above
6.LPA Indeterminate results	A clinical team (Sub county) to review the patient and decide on way forward.			

NOTE:

- **Culture/DST should not be used to confirm / reject GeneXpert results**
- **Every diagnostic test has a risk of providing a false result**
- **Remember that non-test causes of false results are very common**
- **A laboratory test result is only part of the clinical decision making process**
- **Treat the patient's worst case scenario not the test result!**

5.8 External Quality Assessment

External quality assessment (EQA)/proficiency testing program (PT) refers to a system in which laboratory results are scrutinized objectively by an outside agency in order to get a general impression of the standard of laboratory practice and to achieve inter-laboratory comparability. There are different ways of doing EQA i.e. on-site evaluation (supervisory visits), panel testing (PT) and blinded checking. A laboratory can adopt one or more of the stated EQA approaches for every laboratory test performed. This is in line with the clinical laboratory improvement Act CLIA requirement. This helps the laboratory identify errors which are not detected by the internal quality program (IQA) as well as comparing its performance with other laboratories participating in the same. ***(Refer to EQA SOP)***.

5.9 Laboratory Infection Prevention Control

Specimen processing in the laboratory must observe at minimum the key standards of biosafety. ***(Refer to Chapter 10).***

TUBERCULOSIS IN SPECIAL CONDITIONS

6

WHAT'S NEW?

1. Intensified TB Case Finding among PLHIV
   - Symptom-based TB screening using the ICF tool MUST be performed for all PLHIV at every clinic visit to rule out active TB
2. TB diagnosis in PLHIV – TB LAM algorithm for patients with advanced HIV disease
3. HIV Testing in TB patients – updated HIV Testing algorithm
4. Standard package of care for PLHIV
5. Provision of Antiretroviral Therapy (ART) for TB/HIV Co-Infected Patients
   - Timing of ART- patients for TB/HIV co-infected patients
   - Updated Preferred ART Regimens for TB/HIV Co-infection for Patients Newly Initiating 1st Line ART, Patients who Develop TB while Virally Suppressed on 1st Line ART and Patients who Develop TB while Failing 1st Line ART
6. Diagnosis of Diabetes and Pre-Diabetes
   - Thresholds and cut-off points for diabetes and pre-diabetes
7. Bi-directional screening and diagnosis of Diabetes Mellitus and TB
   - Screening and diagnosis of diabetes in people with TB
   - Screening and diagnosis of TB in people with diabetes
8. TB and Mental Health / Substance Dependence
   - All TB co-infected should receive basic screening for depression using the PHQ-9 tool (Annex 6.3a & 6.3b) before initiating TB treatment, and regularly during follow-up, and whenever there is a clinical suspicion of depression.
   - All adult and adolescent TB patients should be screened for alcohol, tobacco and substance dependence before initiating TB treatment and regularly during follow-up using CAGE–AID for adults (Annex 6.1a & 6.1b) and CRAFFT tools for adolescents (Annex 6.2a & 6.2b) respectively.
9. TB in Pregnancy and Lactation – liver function tests indicated at baseline and follow-up.

6.1 Introduction

Tuberculosis incidence, risk, progression and treatment may be altered in particular patient populations such as those with comorbidities (HIV, diabetes, renal disease and hepatic disease), mental illness, substance dependence and pregnant women. This chapter provides information on the unique drug-disease interactions and drug-drug interactions affect the diagnosis and management of tuberculosis in these specific groups of patients.

6.2 TB and HIV CO-Infection

KEY HIGHLIGHTS:

- **HIV testing is recommended for all presumed and confirmed TB cases**
- **All TB patients who are HIV positive should receive the Standard package of care for PLHIV**
- **Symptom-based TB screening using the ICF tool MUST be performed for all PLHIV at every clinic visit**
- **All PLHIV should be assessed for TB Preventive Therapy (TPT) if screened negative for TB.**

6.2.1 Background

TB is the leading preventable cause of morbidity and mortality among people living with HIV. The burden of TB is so closely linked to the HIV epidemic that prevention of HIV must become a priority for TB programs. Patients presenting with signs and symptoms of any of the two diseases should be actively screened for the other and managed appropriately.

The co-infected patients face a dual burden of pills, stigma and discrimination as well as nutritional needs thus providing quality of care is essential. HIV infected individuals are more likely to suffer acute opportunistic infections and develop drug reactions. This therefore calls for close monitoring during management.

6.2.2 TB and HIV Interaction

Interaction of HIV with TB

- Increased lifetime risk of TB from 5-10% to 50%
- Increased rate of progression of new TB infections to disease
- Increased risk of recurrence of previously treated TB
- Increased risk of death from TB
- Increased risk of adverse reactions to anti-TB drugs
- Increased stigma to the two diseases

Interaction of TB with HIV

- Rapid progression of HIV disease
- TB is the leading cause of HIV-related morbidity
- TB is a leading cause of mortality among PLHIV (one-third of all AIDS related deaths are due to TB)
- Increasing TB cases among PLHIV increases the risk of TB transmission in the community regardless of their HIV status.

6.2.3 Intensified TB Case Finding Among PLHIV

TB screening and prevention services should be offered to ALL PLHIV at every clinical visit and to all household contacts of active TB patients. Symptom-based TB screening using the ICF tool **MUST** be performed for all PLHIV at every clinic visit to rule out active TB. Those who screen positive (presumptive TB cases) must complete definitive diagnostic pathways (*refer to table) and patients who screen negative should be evaluated for isoniazid preventive therapy (IPT).

The presentation of TB in HIV infection may be unusual, and may include extra-pulmonary and disseminated forms. However, patients with advanced disease may be symptom-free and have no chronic cough.

The following tables summarize the Pediatric and Adult ICF tools used in TB screening:

Table 6.1: Pediatric Intensified Case Finding Screening Tool (0-14 years of age)

Screening Questions	Y/N
1. Cough of any duration (Y/N)	
2. Fever (Y/N)	
3. Failure to thrive or poor weight gain (Y/N) (based on z-score/BMI)	
4. Lethargy, less playful than usual (Y/N)	
5. Contact with a TB case (Y/N)	
If "Yes" to any of the above questions, suspect TB, examine the child and use the pediatric TB diagnostic algorithm to evaluate for active disease. Rule out underlying conditions, refer if necessary If "No" to all questions, initiate workup for IPT and repeat screening on subsequent visits	

Table 6.2: Adolescent and Adult Intensified Case Finding Screening Tool (≥ 15 years of age)

Screening Questions	Y/N
1. Cough of any duration (Y/N)	
2. Fever (Y/N)	
3. Noticeable weight loss (Y/N) (based on BMI)	
4. Night sweats (Y/N)	

If "Yes" to any question, take a detailed history, examine the patient and do sputum examination if coughing (sputum for GeneXpert and smear, Figure 8.2), and urine TB-LAM if meets criteria (Figure 8.3). Exclude underlying illnesses

If "No" to all questions, initiate workup for IPT and repeat screening on subsequent visits

Note:Draining lymph nodes are often due to TB.

6.2.4 TB Diagnosis in PLHIV

Gene expert RIF/MTB assay is a rapid molecular technique for detection of Mycobacterium Tuberculosis and Rifampicin resistance. It is the recommended first TB diagnostic test amongst PLHIV. Other tools for diagnosis of TB in PLHIV include imaging (X-rays and CT scans) and histology.

Since persons with advanced HIV disease may have disseminated disease which may be missed on GeneXpert testing, it is recommended that PLHIV are tested using lateral flow lipoarabinomannan (LF-LAM) point-of-care urine antigen test. The indications and use of TB-LAM are as per the algorithm in Figure 6.1:

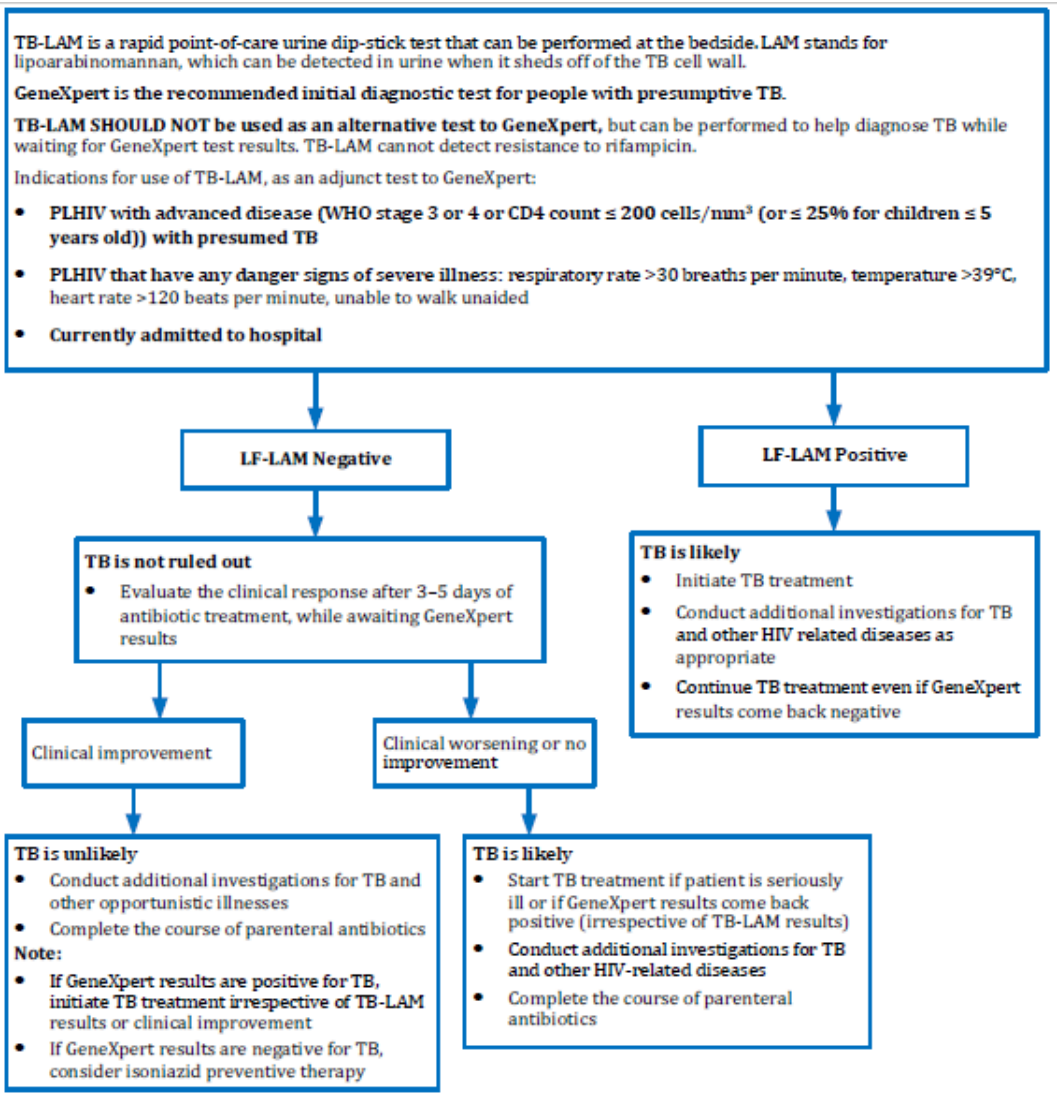


Figure 6.1: TB LAM algorithm

6.2.5 HIV Testing in TB Patients

HIV counseling and testing should be carried out in all presumptive cases as part of the investigations for TB. A diagnosis of HIV infection at the earliest opportunity possible has several benefits including providing standard package of care for HIV positive. HIV testing for TB patients should preferably be done in the Chest clinic. 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 TB patients are not lost during referral and that they do not queue for long while waiting to be attended.

The HIV testing package includes:

- A **pre-test** session
- **HIV test (see Figure 6.2: HIV testing algorithm)** assessment for other health-related conditions or needs (while HIV tests are running),
- A post**-test** session, including assisted partner notification services (aPNS) and child testing
- Referral and **linkage** to other appropriate health services (as part of the post-test session).

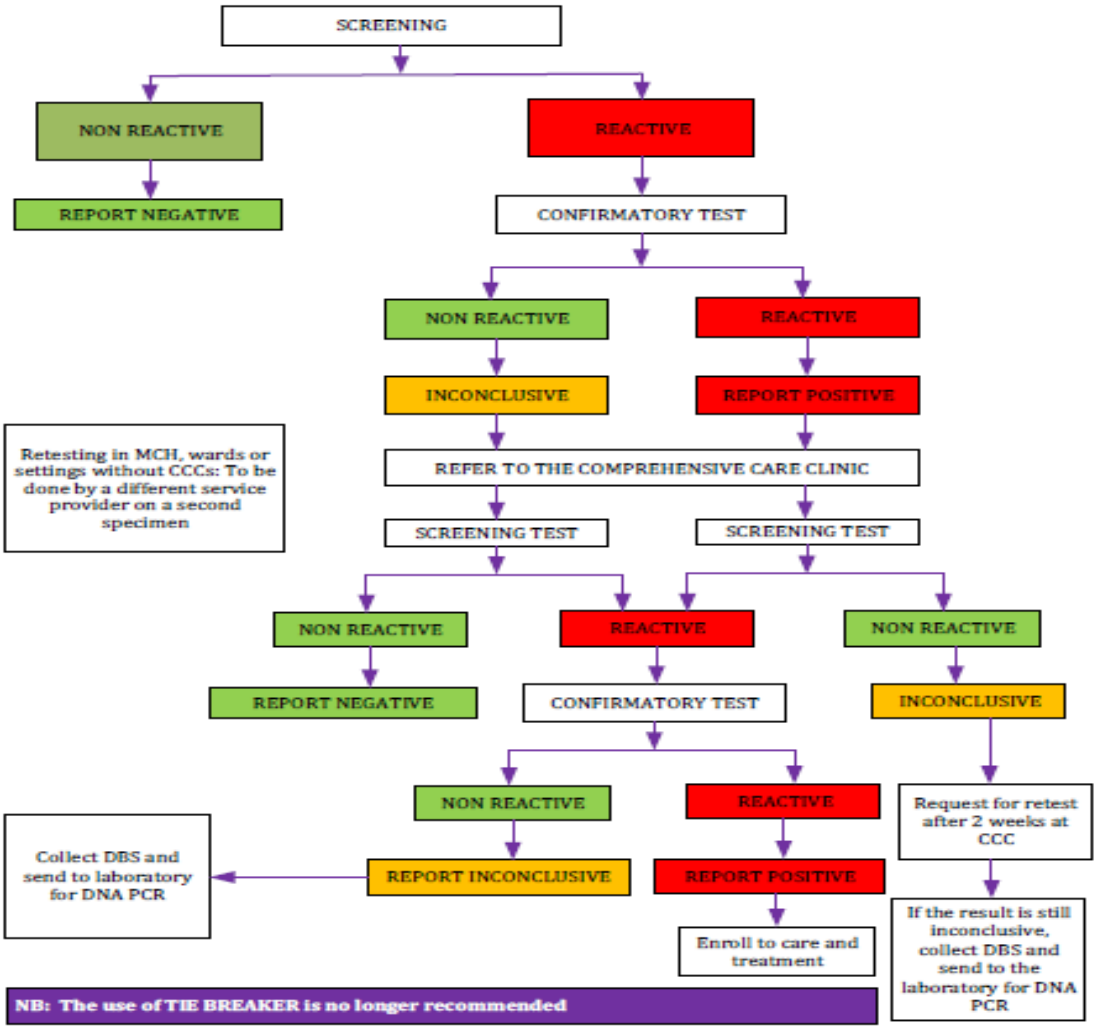


Figure 6.2: HIV testing algorithm

Those who test HIV negative:

- Should be informed about couple discordance and be encouraged to refer their partners for testing
- Should receive behavior change counseling so as to avoid acquisition of HIV infection
- Should be informed that the negative test does not rule out HIV infection and should be encouraged to receive a retest after 12 weeks

Those who test HIV positive:

- Should be initiated on an appropriate regimen based on drug susceptibility and other classification. *Refer to Treatment of Tuberculosis in adults and children*.

6.2.6 Standard Package of Care for PLHIV (9 COMPONENTS)

1. Antiretroviral Therapy

• All PLHIV are eligible for ART irrespective of CD4 cell count or percentage, WHO clinical stage, age, pregnancy status, or comorbidities

• ART should be initiated as soon as the patient is ready to start, preferably within two weeks from time of HIV diagnosis (except for patients with cryptococcal meningitis (5 weeks), or TB meningitis (8 weeks)

2. Positive Health, Dignity, and Prevention, GBV/IPV & Health Education and Counselling

- All patients should be counselled and supported for disclosure of HIV status; partner/family testing and engagement; condom use; family planning; sexually transmitted infections screening; and treatment adherence services.
- All females aged 15-49 years and emancipated minors accessing HIV care services should be screened for Intimate Partner Violence (IPV) as part of the standard package of care.
- All PLHIV should be provided with HIV education and counselling.

3. Screening for and Prevention of Specific Opportunistic Infections

- All PLHIV should receive lifelong Cotrimoxazole preventive therapy (CPT) unless they have allergy to sulfur-based drugs or develop toxicity from CPT.
- During pregnancy, CPT should be initiated irrespective of the gestational age and should continue throughout pregnancy, breastfeeding, and thereafter for life with doses as indicated in Table 6.3:

Table 6.3: Daily Dose of Cotrimoxazole Preventive Therapy

Weight (kg)	If using oral suspension (240mg per 5ml)	If using single strength tablet 480	If using double strength tablet 960 mg
1 – 4	2.5 ml	¼ SS tab	--
5 – 8	5 ml	½ SS tab	¼ DS tab
9 – 16	10 ml	1 SS tab	½ DS tab
17 – 30	15 ml	2 SS tabs	1 DS tab
> 30 20 ml		2 SS tabs	1 DS tab
Adult (any weight)		2 SS tabs	1 DS tab

Note: *If Creatinine Clearance (CrCl) 15-30 ml/min then use 50% of normal recommended dose; if CrCl < 15 ml/min, then Cotrimoxazole should be avoided.*

When Dapsone (as a substitute for CPT) is being used as PCP prophylaxis, it is only recommended for patients in WHO Stage 4 and/or absolute CD4 count ≤ 200 cells/mm3 (or CD4% ≤ 25% for children ≤ 5 years old), and should be discontinued once a patient achieves viral suppression and a sustained CD4 count of > 200 cell/mm3 (or > 25% for children ≤ 5 years old) for at least 6 months.

Dapsone Dosage:

- Available as 25 mg and 100 mg tabs
- Children: 2mg/kg once daily (maximum dose: 100 mg) OR 4 mg/kg once weekly (maximum dose: 200 mg)
- Adults: 100 mg once daily.

All PLHIV should be screened for TB at every visit using the Intensified Case Finding (ICF) tool and assessed for TB Preventive Therapy (TPT) if screened negative for TB (Refer to Chapter 11 on LTBI management)

All adolescent and adult PLHIV with a baseline CD4 count of ≤ 200 cells/mm3 should be screened for cryptococcal meningitis using the serum Cryptococcal Antigen (CrAg) test and managed as per the ART guidelines. This should preferably be a reflex test performed by the laboratory as soon as the low CD4 count is noted

4. Reproductive Health Services

- All PLHIV should be screened for STI at every clinic visit
- Pregnancy status should be determined for all women of reproductive age at every visit and their contraception need determined and met
- All HIV positive women between the ages of 18 - 65 years should be screened for cervical cancer

5. Screening for and Management of Non-Communicable Diseases

- `All PLHIV should be screened for hypertension, diabetes mellitus, dyslipidemia, and renal disease
- `Lifestyle modifications are always the first line of prevention and management for hypertension, diabetes mellitus, and dyslipidemia.

6. Mental Health Screening and Management

- All PLHIV should receive basic screening for depression using the PHQ-9 tool before initiating ART, and annually thereafter, and whenever there is a clinical suspicion
- All adults and adolescents should be screened for alcohol and drug use before initiating ART and regularly during follow-up using CAGE-AID and CRAFFT tools
- All caregivers should also receive baseline and follow-up screening for depression and alcohol/drug use using a PHQ-9 questionnaire.

7. Nutrition Services

- All PLHIV should receive nutritional assessment, counselling, and support tailored to the individual needs of the patients
- All infants irrespective of HIV status should be exclusively breastfed for the first 6 months of life, with timely introduction of appropriate complementary foods after 6 months, and continued breastfeeding up to 24 months or beyond.

For more information on Nutrition in TB refer to Chapter 7.

8. Prevention of Other Infections

- PLHIV (including children) should receive vaccinations as recommended by the National Vaccines and Immunization Programme

9. TB Contact management among co-infected PLHIV

For all bacteriologically confirmed TB/HIV cases, ensure:

- Contact management (Invitation/ Tracing and screening of all contacts)
- TB Preventive Therapy (IPT) for all eligible PLHIV contacts is offered. This includes children living with HIV under the age of 5 with contact to bacteriologically confirmed TB cases *(Refer to LTBI Chapter 11 Section for TB preventive therapy)*

6.2.7 Provision of Antiretroviral Therapy for TB/HIV Co-Infected Patients

Timing of ART for TB/HIV co-infected patients:

a) For all newly diagnosed TB patients not yet on ART

- Start TB treatment immediately
- Initiate ART as soon as anti-TB medications are tolerated, preferably within 2 weeks. For TB meningitis consider delaying ART for up to 8 weeks.
- Monitor closely for IRIS.

b) For all newly diagnosed TB patients who are already on ART

- Start TB treatment immediately
- Continue ART, making any required adjustments to the ART regimen based on drug-drug interactions. Always assess for ART failure in patients who develop TB after being on ART for ≥ 6 months
- Monitor closely for IRIS.

Patients being treated concurrently for TB and HIV require close monitoring for toxicity. MDR TB and HIV co-infection should be managed in settings where close toxicity monitoring and follow up by experienced clinicians is possible. Patients on TDF and aminoglycosides are at high risk for renal toxicity and require close monitoring.

The following tables summarize the preferred ART regimens for TB/HIV co-infection in:

a) Patients newly initiating 1st line ART

b) Patients who develop TB while virally suppressed on 1st line ART

c) Patients who develop TB while failing 1st line ART

d) Recommended Ritonavir Dosing for Super-Boosting LPV/r in Children Taking Rifampicin.

NOTE:

There are updated guidelines for children and adolescents living with HIV on preferred ART regimens as shown in the tables below.

Table 6.4: Preferred ART Regimens for TB/HIV Co-infection for Patients Newly Initiating 1st Line ART

Age	Scenario	Recommendation
Birth – 4 weeks	AZT + 3TC + RAL[1]	Start anti-TB treatment immediately; start ART after 4 weeks of age, once tolerating anti-TB drugs.
4 weeks - <20kgs	ABC/3TC/LPV/r	Super Boost LPV/r[a]
20kgs-35kgs	ABC/3TC/DTG[b]	Give ABC/3TC+DTG (morning) + DTG 50mg (evening) during TB treatment and for additional 2 weeks after TB treatment is completed, then revert back to ABC/3TC+DTGb
>35kg	TDF/3TC/DTG	DTG[b] x2 standard dose BD dosing until 2 weeks after TB treatment is completed, then revert back on OD dosing

[1,a] For children who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is double dose RAL or (DTG once appropriate formulations available) if ≥ 2 years old, if < 2 years old use triple-NRTI regimen of ABC + 3TC + AZT for the duration of TB treatment, then return to ABC + 3TC + LPV/r upon completion of TB treatment.

[b] For children >30kgs and HIV-TB co-infected, use double DTG standard dose and administer BD. Those who cannot tolerate DTG, the alternative is RAL at X2 standard weight-based BD dosing

For patients on these regimens who become viremic consult Regional or National HIV Clinical TWG *(ulizanascop@gmail.com)* or call Uliza Toll-free Hotline **0800 72 48 48.**

Table 6.5: Preferred ART Regimens for Patients who Develop TB while Virally Suppressed on 1st Line ART[1,2,3]

Current Regimen	Age	Recommended substitution
PI/r-based	< 20kgs (above 4 weeks old)	Super-boost LPV/r with additional RTV[4] After completion of TB treatment revert to the recommended first line regimen (ABC + 3TC + LPV/r)
	≥20 kgs	Switch from PI/r to DTG and continue this regimen even after completing TB treatment (give DTG 50 mg BD for duration of rifampicin-containing TB treatment, then reduce to DTG 50 mg once daily 2 weeks after TB treatment is completed). For women and adolescent girls of childbearing potential continue counselling on avoiding pregnancy before use of DTG
EFV-based	Any age	Continue the same regimen for the duration of TB treatment. Consider for regimen optimization after completing TB treatment

Current Regimen	Age	Recommended substitution
RAL-based	All ages	Give double the standard dose of RAL until 2 weeks after completion of rifampicin-based TB treatment, then reduce to standard weight-based dosing
DTG-based 20kgs – 35kgs DTG at x2 standard weight-based BD dosing until 2 weeks after completion of Anti TBs. return to DTG OD 2 weeks after completion of anti TBs		
	>35kgs	Give TDF/3TC/DTG FDC am + DTG 50mg pm for duration of rifampicin-containing TB treatment and for an additional 2 weeks after TB treatment is completed, then revert to TDF/3TC/DTG FDC OD

1. All patients who develop TB after being on ART for ≥ 6 months should be assessed for HIV treatment failure
2. For patients on 2nd line ART, subsequent regimens, or nonstandard drugs who require regimen change because of TB treatment, consult the Regional or National HIV Clinical TWG (Uliza Toll-free Hotline 0800-724848; ulizanascop@gmail.com)
3. NRTIs in the patient's current regimen do not require any adjustments with anti-TB treatment
4. For children on rifampicin based anti-TB regimens, LPV/r should be "super-boosted" by adding additional ritonavir suspension to manage the drug interaction between LPV/r and rifampicin. Two weeks after TB treatment is completed the dosage of LPV/r should return to standard dosing. For children ≥ 2 year who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is RAL (or DTG once appropriate formulations available) at x2 standard weight-based BD dosing until 2 weeks after TB treatment then continue with RAL (or DTG) standard weight-based BD dosing.
5. Guidelines recommend LPV/r for children < 3 years, however some children < 3 years maybe on NVP due to LPV/r toxicity, consult the Regional or National HIV Clinical TWG (Uliza Toll-free Hotline **0800 72 48 48**; **ulizanascop@gmail.com**)

NOTE:

a) **Studies of RAL in the treatment of pediatric TB are ongoing. Initial data from older cohorts suggest that a double dose of RAL is safe and effective in the treatment of HIV in children receiving TB therapy containing rifampicin. However, there is no data on the treatment of TB in children under 2 years of age using RAL. Given the highly variable pharmacokinetics in this age group, caution is advised and routine VL monitoring must be followed**

b) **DTG formulations such as 5 mg and 10 mg may become available within the country and will be the preferred option for TB/HIV patients rather than RAL**

Table 6.6: Recommended ART Regimens for Patients who Develop TB while Failing 1st Line ART

Age/Scenario	First-line ART	Second-line ART
<20kgs	PI/r-based 1st line	Start anti-TB immediately. Super-boost the LPV/r 2 while following the viral load monitoring algorithm (2018 ART guidelines Figure 6.5), including assessing for and addressing reasons for treatment failure. Once treatment failure is confirmed and patient is ready to switch to 2nd line, switch to DST-based 2nd line[2]
	ABC (or AZT) + 3TC + EFV	Start anti-TB immediately If <3 years, switch to AZT + ABC + 3TC while following the viral load monitoring algorithm, including assessing for and addressing reasons for treatment failure If > 3 yrs and on EFV, continue current regimen while following the viral load monitoring algorithm, including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient ready to switch to 2nd line, switch to AZT + 3TC + LPV/r (with super-boosted LPV/r[2] until 2 weeks after completion of TB)
20 - 35kgs	ABC (or AZT) + 3TC + DTG (or EFV)	Start anti-TB immediately Continue current regimen (if on DTG, then use double dose until 2 weeks after TB treatment completed) while following the viral load monitoring algorithm, including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient ready to switch to 2nd line, switch to AZT + 3TC + LPV/r (with super-boosted LPV/r[2] until 2 weeks after completion of TB treatment). If patient was on AZT-containing 1st line then switch to ABC in 2nd line
	PI/r-based 1st line	Start anti-TB immediately Super-boost the LPV/r[2] while following the viral load monitoring algorithm (2018 ART guidelines Figure 6.5), including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient is ready to switch to 2nd line, switch to DRT-based 2nd line

Age/Scenario	First-line ART	Second-line ART
≥ 15 years (or ≥ 35 kg body weight)	TDF (or ABC or AZT) + 3TC + DTG	Start anti-TB immediately Add DTG 50 mg pm to their current regimen while following the viral load monitoring algorithm (2018 ART guidelines Figure 6.5), including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient ready to switch to 2nd line, switch to AZT + 3TC + ATV/r (if on TDF or ABC in 1st line) and change to rifabutin-based anti-TB treatment. If patient was on AZT-containing 1st line then switch to TDF in 2nd line
	TDF (or ABC or AZT) + 3TC + EFV (or NVP)	Start anti-TB immediately Continue current regimen (if on NVP, switch to EFV) while following the viral load monitoring algorithm (Figure 6.5), including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient ready to switch to 2nd line, switch to AZT + 3TC + ATV/r (if on TDF or ABC in 1st line) and change to rifabutin-based anti-TB treatment[1]. If patient was on AZT-containing 1st line then switch to TDF in 2nd line
	PI/r-based 1st line	Start rifabutin-based anti-TB therapy immediately or consult if rifabutin unavailable[1] Continue current regimen while following the viral load monitoring algorithm (Figure 6.5), including assessing for and addressing reasons for treatment failure Once treatment failure is confirmed and patient is ready to switch to 2nd line, Switch to DRT-based 2nd line
Pregnant or Breastfeeding	Consult the Regional or National HIV Clinical TWG urgently (Uliza Toll-free Hotline 0800 72 48 48; *ulizanascop@gmail.com*)	
HIV/HBV Co-infection	Always maintain TDF in second-line instead of switching to a different NRTI and instead of adding an additional NRTI	

[1] For patients on 2nd line ART, subsequent regimens, or nonstandard drugs who require regimen change because of TB treatment, consult the Regional or National HIV Clinical TWG (Uliza Toll-free Hotline 0800 72 48 48; *ulizanascop@gmail.com*)

[2] Use "super-boosted" LPV/r by adding additional ritonavir suspension to manage the drug interaction between LPV/r and rifampicin (see Table 6.7 for dosing recommendations). Two weeks after TB treatment is completed the child should go back to standard LPV/r dosing. For children ≥ 2 years who cannot tolerate LPV/r + RTV (usually because of GI side-effects), the alternative regimen is RAL (or DTG once appropriate formulations available) at x2 standard weight-based BD dosing until 2 weeks after TB treatment then continue with RAL (or DTG) standard weight-based BD dosing.

Rifampicin causes drug-drug interactions by cytochrome (CYP) p450 induction and reduces LPV/r exposure by approximately 90% when used at the normal 4:1 ratio. Ritonavir is an ideal pharmacologic enhancer because it inhibits cytochrome CYP3A4 in the intestines and in the liver, thus increasing LPV/r maximal plasma concentration and half-life. This effect is magnified when LPV/r is super-boosted with Ritonavir for a 1:1 ratio, thus allowing for use of Rifampicin based TB treatment in children. In adults, the drug interaction due to Rifampicin is avoided by using Rifabutin instead or using DTG twice daily dosing instead of Protease Inhibitor (PI) based ART.

The table below shows the dosing of Ritonavir for super-boosting LPV/r in children who need TB treatment while on PI based ART:

Table 6.7: Ritonavir Dosing for Super-Boosting LPV/r in Children Taking Rifampicin

Weight Range (kg)	Standard Dosing of Lopinavir/ritonavir (LPV/r) (Twice Daily)				Additional dosing of ritonavir for children taking rifampicin (Twice Daily)
	LPV/r 80/20 mg/ml solution	LPV/r 40/10mg pellets (number of pellets)	LPV/r 100/25mg tablets	LPV/r 200/50mg 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 ml BD	2 BD	Not recommended	Not recommended	1 ml BD
6 - 9.9	1.5 ml BD	3 BD	Not recommended	Not recommended	1 ml BD
10 - 13.9	2 ml BD	4 BD	2 a.m. 1 p.m.	Not recommended	1.5 ml BD
14 - 19.9	2.5 ml BD	5 BD	2 BD	1 BD	2 ml BD
20 - 24.9	3 ml BD	6 BD	2 BD	1 BD	2.5 ml BD
25 - 29.9	Not recommended	7 BD	3 BD	2 am 1 pm	4 ml am 2 ml pm
30-34.9	Not recommended	8 BD	3 BD	2 am 1 pm	4 ml am 2 ml pm
≥35	Not recommended	10 BD	4 BD	2 BD	4 ml BD

6.2.8 Appointment Management

Schedule follow up for stable versus unstable TB patients:

1. **For Stable patients:**
    - In the intensive phase: Clinic appointments every 2 weeks (Twice a month)
    - In the continuation phase: Clinic appointments every 4 weeks (monthly)

2. **For unstable patients**, more frequent appointments should be booked for closer monitoring.

6.2.9 Adherence Preparation, Monitoring & Support

Following a TB diagnosis, patients should be supported using an individualized patient management plan that includes establishing appropriate adherence support interventions. This is essential for the patient's well-being and good health outcomes. To prevent non adherence and default from treatment the following measures are essential:

1. Structural interventions including:
    - Assessment of client readiness to initiate and continue with treatment
    - Assessment for risk factors for non-adherence eg alcohol abuse
    - Appropriate treatment delivery settings eg Differentiates Care
    - Linkage to community based services and social support programmes
    - Outline a return to care package
    - Adherence monitoring through patient self-reporting and pill counts
2. TB health education and literacy package:
    - Health talks and treatment literacy
    - One on one patient education sessions
3. Identification of treatment supporter/DOTs supporter
4. Address stigma and discrimination issues
    - Conduct stigma assessment and support using an individualized TB treatment plan. Stigma may arise from the patient themselves, family members, the community, and other patients
5. Defaulter prevention and tracking
    - Use of appointment management system
    - SMS reminders
    - Handling treatment interruptions

6.2.10 Establishing TB/HIV Collaborative Activities

For effective implementation of TB/HIV collaborative activities, there should be adequate coordination at county, sub county and facility level. The county and sub county TB/HIV coordinating committees need to constantly conduct supportive supervision to identify strengths and weaknesses and motivate staff.

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

Collaborative TB/HIV activities which need to be implemented in facility settings are summarized in the table below:

Table 6.8: Collaborative TB/HIV Activities

Objective/ Activity
A. **To enhance TB/HIV collaboration (5 I's)** • Intensified TB case finding • TB Preventive Therapy • TB infection control in healthcare settings • TB/HIV service Integration • Immediate ART initiation
B. **To decrease the burden of TB in PLHIV** • Enhance early diagnosis through ICF • Facilitate immediate TB treatment • Synchronization of appointments • Strengthen inter/intra facility referrals
C. To decrease the burden of HIV in TB patients 1. HIV testing and counselling for confirmed and presumed cases 2. HIV combination prevention 3. Cotrimoxazole preventive therapy 4. HIV/AIDS care and support 5. Antiretroviral therapy to TB/HIV co-infected patients

6.3 TB and Diabetes Mellitus

KEY HIGHLIGHTS:

- **All adult TB patients should be screened for diabetes at TB treatment initiation**
- **Patients with diabetes should be screened for TB at every clinic visit using TPT/ICF symptom questionnaire**
- **Gene Xpert MTB/RIF is the preferred diagnostic test for TB in diabetes**
- **Treatment of TB in patients with diabetes is similar to that in patients without diabetes**
- **TB treatment is at chest/TB clinic while comprehensive diabetes management should be in diabetes clinic.**
- **However, patient education on lifestyle modification and basic monitoring of treatment for diabetes be also carried out in chest/TB clinic**
- **Insulin is the drug of choice where blood sugar control is not attained, severe TB, renal disease or liver disease**
- **Closely monitor treatment response, adherence and adverse reactions to TB and diabetes**

6.3.1 Introduction

Diabetes mellitus is a serious and usually life-long condition characterized by hyperglycemia, as a result of defects in insulin secretion, insulin action or both. Insulin is secreted as a hormone from the endocrine pancreas to regulate the level of glucose in the body. The prevalence of diabetes is markedly increasing in every country, including sub-Saharan Africa.

Diabetes is classified into the following general categories:

1. **Type 1 diabetes** – due to autoimmune pancreatic -cell destruction, usually leading to absolute insulin deficiency and accounts for 5 – 10% of diabetes
2. **Type 2 diabetes** – due to a progressive loss of adequate pancreatic -cell insulin secretion in the background of insulin resistance; accounts for over 90% of diabetes
3. Specific causes of diabetes such as:
   - monogenic diabetes syndromes – maturity onset diabetes of the young
   - diseases of the exocrine pancreas – cystic fibrosis, chronic pancreatitis
   - endocrine diseases – Cushing's syndrome, acromegaly
   - drug-induced diabetes – systemic glucocorticoids, antipsychotics
4. Gestational diabetes – diagnosed in the second or third trimester

Diabetes can result into many serious complications including microvascular and macrovascular complications. Globally, 15% of tuberculosis cases are estimated to be attributable to diabetes. Among diabetic patients, the risk of TB increases. Diabetes increases the risk of developing active tuberculosis 2 to 3-fold and is associated with worse tuberculosis treatment outcomes. Diabetes may also potentiate the adverse effects of some anti-TB drugs, especially renal dysfunction and peripheral neuropathy.

On the other hand, tuberculosis disease, can lead to stress-induced hyperglycemia and unmask diabetes in susceptible individuals. Some anti-TB drugs like Isoniazid also have hyperglycemic effects. Additional ways that the two diseases interact are as shown in the table below.

Table 6.9: Interactions between Diabetes Mellitus and Tuberculosis

<table>
<tr><th>Effect of Diabetes Mellitus on TB</th><th>Effect of TB on Diabetes Mellitus</th></tr>
<tr><td>On incidence and prevalence
- increases risk of TB 2-3 times
- increases risk of MDR-TB</td><td rowspan="4">- TB may unmask diabetes
- TB increases glucose intolerance and hyperglycemia
- TB impairs glycemic control</td></tr>
<tr><td>On clinical presentation
- TB may present atypically
- TB may progress faster
- TB may present with more chest and systemic symptoms
- TB may present with more frequents and higher grade smear/culture positivity</td></tr>
<tr><td>On response to TB treatment
- prolonged smear/ culture positivity
- higher risk of adverse drug reactions eg hepatitis, renal toxicity, GIT effects</td></tr>
<tr><td>On TB treatment outcome
- increased risk of death
- increased risk of treatment failure
- increased risk of loss to follow-up
- increased risk of relapse</td></tr>
<tr><td colspan="2">On post-TB complications
- extensive TB disease, late presentation & delayed diagnosis/treatment initiation may increase risk of post-TB complications like chronic obstructive and chronic restrictive lung disease</td></tr>
</table>

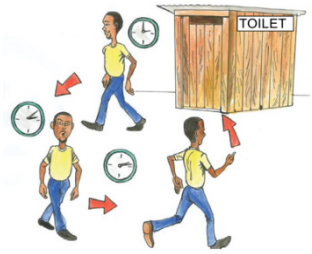
6.3.2 Risk factors for diabetes mellitus

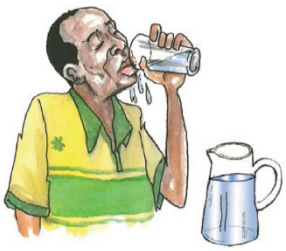
Table 6.10: Risk Factors for Diabetes Mellitus

Non-modifiable risk factors for DM	Modifiable risk factors for DM
Age (increasing age >40 years)	Overweight/obesity
Gender (higher in males)	Physical inactivity
Family history of diabetes	Dietary factors (red meat, sugary beverages)
Genetic markers	Alcohol consumption and tobacco use
Ethnicity (higher in Africans and Asians)	Hypertension
Previous gestational diabetes	Prenatal/early life influences (prematurity)

6.3.3 Symptoms of diabetes

Figure 6.3: Symptoms of Diabetes

<table>
<tr><th colspan="3">The Classic Symptoms of DM are:</th></tr>
<tr><td> 

Polyuria– need to urinate frequently</td><td> 
Polydipsia – increased thirst and fluid intake</td><td> 
Tiredness and fatigue</td></tr>
<tr><td> 
Unexpected weight loss</td><td></td><td></td></tr>
<tr><th colspan="2">Other key symptoms of DM include:</th><th></th></tr>
<tr><td> 

Blurred vision</td><td> 
Increased appetite/ Extreme hunger</td><td> 
Slow healing of wounds</td></tr>
</table>

6.3.4 Diagnosis of Diabetes Mellitus and pre-Diabetes

Diabetes is a chronic progressive disease and its diagnosis is not always straightforward. The threshold or cut-off values for diagnosis are largely based on the levels at which the risk of complications increase. Diabetes may thus be identified anywhere along the spectrum of clinical scenarios.

The WHO recommends the following four tests for the diagnosis of diabetes and pre-diabetes:

1. Oral glucose tolerance test (OGTT)
2. Fasting blood glucose (FBG)
3. Glycosylated haemoglobin (HbA1c)
4. Random blood glucose in the presence of signs and symptoms of DM

The table below gives the cut-off points for diagnosis of diabetes and pre-diabetes:

Table 6.11: Thresholds and cut-off points for diabetes and pre-diabetes

Diagnostic Test	Normal Values	Pre-diabetes	Diabetes
Fasting blood glucose (FPG)	>3.5 to <5.5 mmol/L	5.6 to 6.9 mmol/L	>7.0 mmol/L
Two-hour blood glucose (2-h PG) during oral glucose tolerance test (OGTT) using 75gm glucose in water	<7.8 mmol/L	7.8 to 11.1 mmol/L	>11.1 mmol/L
Glycated haemoglobin A1c (HbA1c)	<42 mmol/L (<6.0%)	42-47 mmol/L (6.0-6.4%)	>47 mmol/L (>6.4%)
Random blood glucose	>3.5 to 7.8 mmol/L	7.8 to 11.0 mmol/L	>11.1 mmol/l if classic symptoms of diabetes or hyperglycaemic crisis are present.

Values are based on plasma glucose (venous) samples.

The diagnosis of DM is made using these thresholds and cut-off points based on whether the person investigated is *symptomatic* (for example, polyuria, polydipsia, unexplained weight loss) or *asymptomatic*.

NOTE:

1. "Fasting" is defined as no caloric intake for at least eight hours.
2. "OGTT" The test should be performed as described by World Health Organization (WHO), using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in 250 ml water ingested over five minutes.
3. "Random" (casual) is defined as any time of day, without regard to time of last meal. The classic symptoms of hyperglycaemia include polyuria, polydipsia and weight loss. "Hyperglycaemic crisis" refers to diabetic ketoacidosis or hyperosmolar nonketotic hyperglycaemia.
4. Lifestyle modifications include weight management, adequate physical exercise and low carbohydrate, low fat, high fibre diet.

6.3.5 Bi-directional screening and diagnosis of Diabetes Mellitus and TB

All confirmed/ diagnosed TB patients should be screened for diabetes at the time of diagnosis or registration for TB.

Additionally, all people diagnosed with Diabetes Mellitus should be screened for Tuberculosis at each clinic appointment.

The following two algorithms are used in bi-directional screening.

Figure 6.4: Screening and diagnosis of diabetes in people with TB

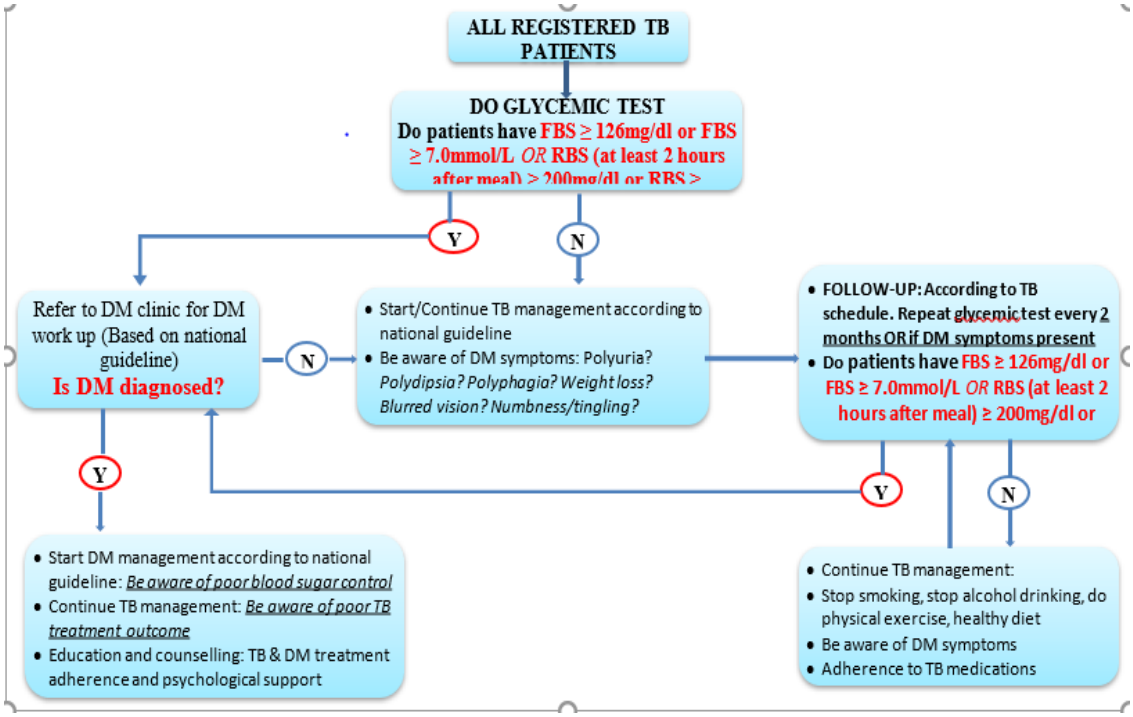
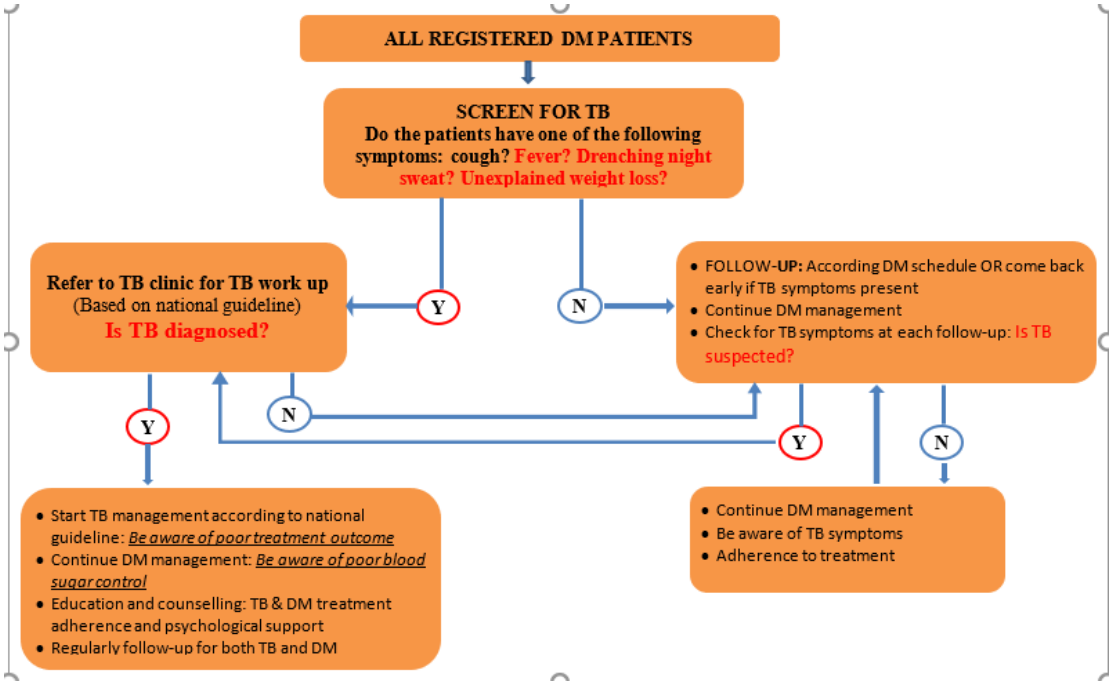


Figure 6.5: Screening and diagnosis of TB in people with diabetes



***TB preventive therapy is not recommended for patients with diabetes.*

6.3.6 Management of Diabetes Mellitus and TB

The management of diabetes is aimed at reducing short- and long-term complications related to the disease. The management of diabetes consists of lifestyle modification i.e. diet, weight loss, physical activity, smoking cessation, avoiding alcohol, administration of glucose lowering agents, instituting measures to reduce risk of cardiovascular and related complications, and management of existing complications like diabetic foot, neurological and eye problems.

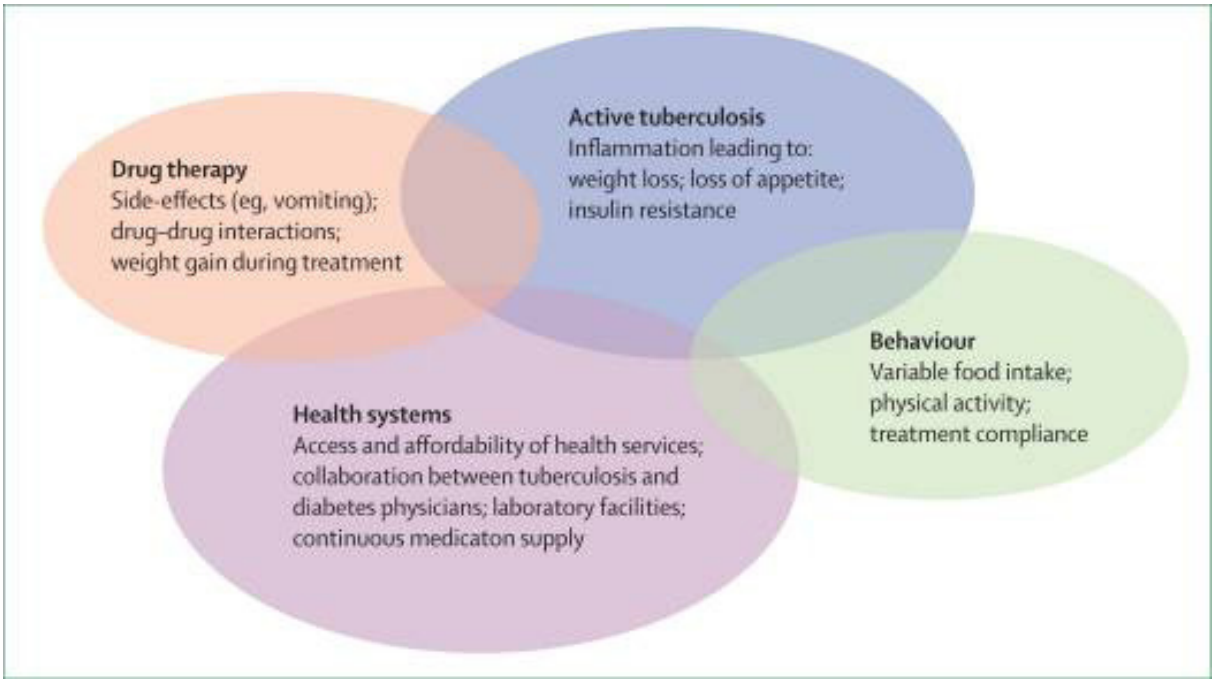
In patients with both diabetes and TB, the priority is to treat TB disease while at the same time controlling the blood glucose levels. In such patients, TB should be treated at the chest/TB clinic while diabetes should be treated in conjunction with diabetes specialists. However, the chest clinicians should be able to give patient education geared towards lifestyle modification, ensure that the patient is adherent to the glucose lowering medications, and be aware of the patient's blood glucose levels. The comprehensive management of diabetes should be left with the diabetes specialists. To minimize transmission of TB it is important to minimize visits to the diabetes clinics especially in the first 2 weeks to 2 months of TB treatment for bacteriologically-confirmed patients.

Treatment of drug sensitive and drug resistant TB is similar in persons with or without diabetes. Rifampicin may cause new-onset hyperglycemia or worsen glycemic control in existing diabetes. **Insulin is the preferred treatment in early stages of TB treatment, in severe TB and in renal or liver impairment. Note that insulin requirements might increase while on Rifampicin.** Later the patients can be switched to Oral Glycemic

Agents (OGLAs) with caution once the disease has settled. Metformin is preferred as the OGLA for patients with TB since it is not metabolized by cytochrome P450 enzymes compared to other OGLAs which have drug-drug interactions with rifampicin (due to induction of cytochrome P450 enzymes) that limit their use e.g. sulfonylureas.

Optimal glycemic control might improve outcomes of tuberculosis treatment and prevent many of the complications associated with diabetes. However, tuberculosis often leads to decreases in appetite, bodyweight, and physical activity, all of which might affect glucose homoeostasis. TB treatment can have opposite but unpredictable effects by decreasing inflammation, and increasing appetite, body weight, and physical activity as shown in the figure below.

Figure 6.6: Factors affecting glycemic control for patients with diabetes during TB treatment



6.3.7 Comprehensive Diabetes management

The goals of management of DM include controlling blood glucose as well as reducing short-term and long-term complications such as cardiovascular disease, eye problems and foot amputations. Personalized pragmatic glycemic targets might be needed that account for various factors, such as severity and prognosis of a patient's TB disease, risk of adverse events such as hypoglycemia, duration of diabetes, comorbidities, age, patient capabilities and treatment preferences, and available resources. Increased vigilance is needed in monitoring treatment response to both the anti-TB and diabetes treatment by doing the routine sputum follow-ups, blood glucose levels, renal function, monitoring adherence, adverse events and other complications.

Poorly controlled Type 1 diabetes increases the risk of stunted growth and diabetes complications, including diabetic ketoacidosis. Comprehensive management of Type 1 diabetes includes the following:

1. Insulin treatment – required for all type 1 diabetes patients
2. Blood glucose monitoring
3. HBA1c monitoring
4. Nutritional management and physical activity
5. Diabetes education
6. Psychosocial support

Insulin comes in two broad categories as shown below:

1. Human insulin – short acting (regular or soluble), intermediate (Neutral protamine Hagedorn insulin, Humulin N, Insulatard), and pre-mix short-acting (regular) and intermediate-acting (NPH) insulins usually in the combination 70/30 (Mixtard, Humulin) or 50/50 (Humulin 50/50)
2. Analogue insulin – rapid acting (Humalog, Novo rapid, Apidra), long acting (Levemir, Lantus) and pre-mix (Humalog 75/25, NoVo mix 70/30)

The following figure summarizes the mode of action and administration of the various types of insulin currently available.

Figure 6.7: Types of Insulin, mode of action and administration of Insulin

TYPE OF INSULIN		ONSET OF ACTION	PEAK OF ACTION	DURATION OF ACTION	WHEN TO ADMINISTER
RAPID	Humalog or Lispro	< 15 min	60-90 min	3-5 hrs	• Inject 10-15 min before mealtime • Typically used in conjunction with longer-acting insulin.
	Novolog or Aspart	< 15 min	60-120 min	3-5 hrs	
	Apidra or Glulisine	< 15 min	60-90 min	1-2.5 hrs	
SHORT	Regular (R) Humulin, Actrapid or Novolin	30-60 min	2-5 hrs	6-8 hrs	• Inject at least 20-30 minutes before mealtime
	Velosulin	30-60 min	2-3 hrs	2-3 hrs	
INTERMEDIATE	NPH (N)	1-2 hrs	4-12 hrs	18-24 hrs	• Commonly used twice daily • Often combined with rapid- or short-acting insulin
	Lente (L)	1-2.5 hrs	3-10 hrs	18-24 hrs	
LONG	Ultralente (U)	30 min- 3 hrs	10-20 hrs	20-36 hrs	• Covers insulin needs for 24 hrs • If needed, often combined with rapid- or short-acting insulin
	Lantus or Glargine	1-1.5 hrs	No Peak	20-24 hrs	
	Levemir or Determir	1-2 hrs	6-8 hrs	Up to 24 hrs	
PRE-MIXED	Humulin 70/30	30 min	2-4 hrs	14-24 hrs	• Combination of intermediate- and short-acting insulin • Commonly used twice daily before mealtime
	Novolin 70/30	30 min	2-12 hrs	Up to 24 hrs	
	Novolog 70/30	10-20 min	1-4 hrs	Up to 24 hrs	
	Humulin 50/50	30 min	2-5 hrs	18-24 hrs	
	Humalog 75/25	15 min	30 min-2.5 hrs	16-20 hrs	

Comprehensive management of Type 2 diabetes includes the following:

1. Treatment of hyperglycemia and hypoglycemia
2. Treatment of hypertension and dyslipidemia
3. Prevention and treatment of micro-vascular complications (retinopathy, neuropathy, nephropathy, sexual dysfunction and diabetic foot)
4. Prevention and treatment of macro-vascular complications (coronary artery disease, cerebrovascular disease and peripheral vascular disease)

Lifestyle changes and nutritional management complement pharmacological treatment of hyperglycemia in diabetic patients. Oral pharmacotherapy is indicated for patients with Type 2 diabetes when an individual's glycemic targets are not met by the combination of dietary modifications and physical activity/exercise. The choice of Oral Glucose Lowering Agents (OGLAs) should depend on the patient's characteristics, lifestyle, degree of glycemic control, cardiovascular and renal risks, access to drugs, economic status and agreement between the doctor and the person living with diabetes.

Table 6.12 below summarizes the characteristics of the OGLAs which are frequently used in controlling glycaemia in diabetes care. The list is not exhaustive but includes agents that are most commonly used in Kenya.

Table 6.12: Oral glucose lowering agents, Side Effects and Contraindications

Drug	Major Side Effect	Contraindication / Precautions
A. Sulphonylureas – stimulate the pancreas to release insulin (regardless of time and glucose levels		
Glibenclamide	Hypoglycemia, weight gain, skin rashes	Caution in liver and renal disease
Gliclazide MR	Hypoglycemia, weight gain, skin rashes	Pregnancy, caution in liver disease
Glimepiride	Hypoglycemia, weight gain, skin rashes	Pregnancy, caution in liver and renal disease
Glipizide	Hypoglycemia, weight gain, skin rashes	Pregnancy, caution in liver and renal disease
B. Biguanides – cause reduction glucose production in liver and peripheral insulin resistance		
Metformin	Nausea, diarrhea, abdominal bloating	Renal failure (GFR <30 ml/min), heart failure stage 3 or 4 and liver failure
C. Thiazolidinediones – improve insulin sensitivity in muscle, adipose tissue and liver, reduce glucose output from liver and change fat distribution by decreasing visceral fat and increasing peripheral fat		
Pioglitazone	Liver impairment, fluid retention weight gain, dilutional anemia, osteoporosis	Heart failure, liver failure; pregnancy and bone fractures

Drug	Major Side Effect	Contraindication / Precautions
D. Meglitinides – stimulate the pancreas to release more insulin		
Repaglinide	Hypoglycemia	Caution in liver disease (metabolized primarily in the liver)
E. Alpha glucosidase inhibitors – slow digestion of complex sugars (sucrose and starch) by and therefore delay glucose absorption, leading to slow post-meal rise in blood glucose		
Acarbose	Flatulence, diarrhea, abdominal pain	Renal failure (GFR <25 ml/min)
F. Dipeptidyl-peptidase-4 inhibitors – increase incretin hormones causing increased insulin release and decreased glucagon secretion from the pancreas (leading to reduced hepatic glucose production)		
Sitagliptin	Headaches, skin reactions, pancreatitis	Allergic reaction, pancreatitis
Vildagliptin	Headaches, skin reactions, pancreatitis	Allergic reaction, pancreatitis
Saxagliptin	Headaches, skin reactions, pancreatitis	Allergic reaction, pancreatitis, caution in heart failure
Linagliptin	Headaches, skin reactions, pancreatitis	Allergic reaction, pancreatitis
G. Sodium-glucose co-transporter-2 inhibitors – suppress renal glucose reabsorption resulting in increased urinary glucose excretion		
Dapagliflozin	Genital and urinary tract infections	Dose adjustment in renal disease
Empagliflozin	Genital and urinary tract infections	Dose adjustment in renal disease
H. Glucagon-like peptide-1 receptor agonists - increase insulin secretion while inhibiting glucagon release and delays gastric emptying with subsequent decreased food intake		
Liraglutide	Nausea, vomiting	Medullary thyroid carcinoma
Exenatide	Nausea, vomiting	Medullary thyroid carcinoma

In initiating treatment for people living with type 2 diabetes, the use of HbA1c test is important. Table 6.7 provides a guide for initiating therapy using the HbA1c levels.

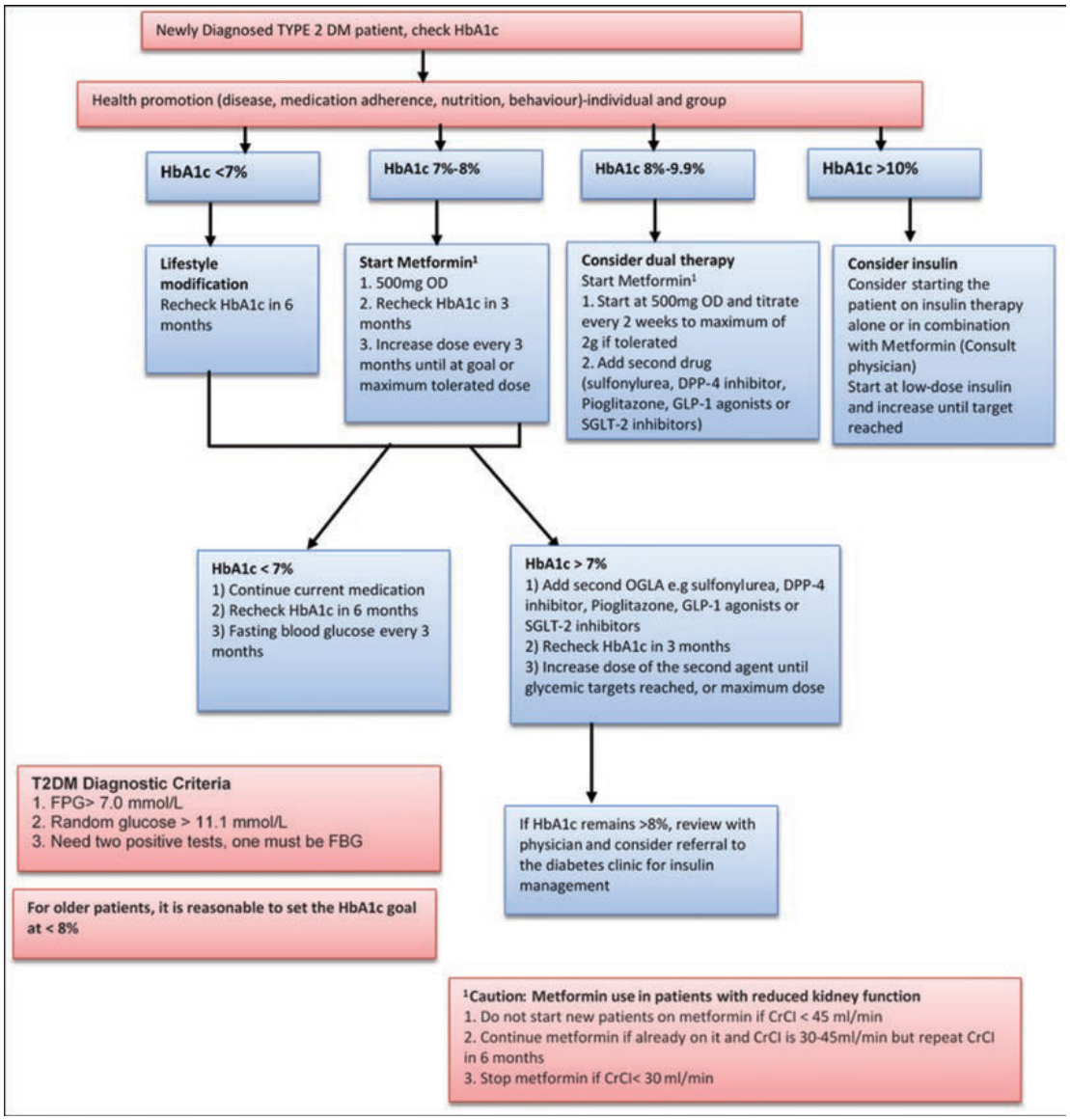
As patients with diabetes are at increased risk of TB disease, the general principles of Infection Prevention and Control of TB transmission should be applied in diabetes clinics. These include administrative, environmental and personal protection measures.

6.3.7 Recording and reporting for diabetes mellitus and tb

Screening for and diagnosis of diabetes in patients with TB should be recorded in the primary tools for managing patients with TB including TB patient record card (TB5), treatment register (TB4), patient appointment cards and TIBU. Screening for and

diagnosis of TB in patients with diabetes should be recorded in patient files/charts and registers used in diabetic outpatient clinics.

Figure 6.7: Medical management of Type 2 Diabetes Based on HbA1c levels



6.4 TB in mental health and substance dependence

The risk of active TB is substantially elevated in persons who consume more than 40 g alcohol per day; most likely due to depressed immune system. Alcohol is also injurious to the liver in various ways including:

1. Alcohol-associated fatty liver (steatosis) – via reduced oxidation of hepatic fatty acids and increased lipogenesis
2. Alcohol-associated steatohepatitis – via impaired cell mediated immunity with; persistent hepatic inflammation causing loss of hepatic regeneration capacity and progressive fibrosis

Anti-TB drugs may also lead to drug induced liver injury. Alcohol use and abuse increase oxidative stress, while the combination of alcohol and anti-TB drugs may lead to a higher risk of hepatic reactions. It is advisable therefore, to encourage patients on anti-TB treatment to avoid alcohol use entirely or at least during treatment.

Cigarette smoking is the leading preventable cause of mortality. Tobacco smoking should be strongly discouraged in TB patients since it is injurious to body organs in various ways:

- Smoking tobacco has been associated with several cancers in various sites such as lung, bladder, colorectal, liver, kidney, head and neck
- Tobacco smoking can cause cardiovascular disease and death due to coronary vasoconstriction, increased hypercoagulability, dyslipidemia, and endothelial dysfunction
- Cigarette smoking is the most important risk factor for COPD and is implicated as well in interstitial lung diseases and pulmonary fibrosis
- Cigarette smoking confers a relative risk of about 1.5 to 2 for the development of TB while also is a risk factor for TB relapse and mortality.
- Smoking increases risk of developing type 2 DM, osteoporosis in women, delayed wound healing and peptic ulcer disease

Patients with TB may suffer from mental disorders such as depression, anxiety disorders and post-traumatic stress disorder. This may be compounded by the fact that TB and mental illnesses have similar underlying factors such as poverty, malnutrition and stress. Persons with mental illnesses and substance use disorders are more likely to be exposed to TB, develop active TB, delay seeking care, miss doses and default from treatment. There is also a greater risk for advanced disease, drug resistance, treatment failure, death, and community transmission (prolonged infectiousness). Incidence of mental and substance abuse disorders in TB patients may occur due to various reasons:

- As a result of the diagnosis – linked to stigma
- As a result of TB medications
- Exacerbation of current diagnosed mental health concerns
- As a new presentation of undiagnosed mental health concerns

Patients receiving TB treatment should be encouraged to abstain from alcohol and/or other substances. Strict DOT should be implemented for patients with substance dependence at high risk of abandoning treatment. Adherence support should be established to avoid treatment interruption as much as possible to avoid development of drug resistant TB.

Further recommendations for mental health and substance dependence screening in TB patients include:

- All TB co-infected should receive basic screening for depression using the PHQ-9 tool (Annex 6.3a and b) before initiating TB treatment, and regularly during follow-up, and whenever there is a clinical suspicion of depression.

- All adult and adolescent TB patients should be screened for alcohol, tobacco and substance dependence before initiating TB treatment and regularly during follow-up using CAGE–AID for adults (Annex 6.1a and b) and CRAFFT tools for adolescents (Annex 6.2a and b) respectively.
- All caregivers for children and adolescents should also receive baseline and follow-up screening for depression and alcohol/drug use using the above mentioned tools.

6.5 TB and liver disease

Patients with history of liver disease can receive anti-TB drug regimens provided there is no clinical evidence of severe chronic liver disease, hepatitis virus carriage (especially Hepatitis C), recent history of acute hepatitis or excessive alcohol consumption. Hepatotoxicity following use of anti-TBs however, may be more common in these patients and close monitoring of liver enzymes is advised.

Pyrazinamide is the most hepatotoxic anti-TB agent, while rifampicin is least likely to cause hepatocellular damage, although it is associated with cholestatic jaundice with elevations in serum bilirubin and alkaline phosphatase concentrations. There is also overlap in the pattern of liver injury caused by rifampin, isoniazid, and pyrazinamide; all three may be associated with elevations in serum transaminase concentrations. Patients should be counseled to avoid use of alcohol and drugs associated with hepatotoxicity (such as Paracetamol).

Patients should be educated about the signs and symptoms of hepatic toxicity; these include anorexia, nausea, vomiting, dark urine, icterus, rash, pruritus, fatigue, fever, abdominal discomfort (particularly right upper quadrant discomfort), easy bruising or bleeding, and arthralgias. All symptomatic patients should be evaluated clinically and have liver function tests performed.

In patients with unstable or advanced liver disease, liver function tests should be conducted at treatment initiation to determine a baseline and determine severity. Clinical judgement is necessary where a patient with TB has a concurrent acute hepatitis that is unrelated to TB or anti-TB treatment. In some cases, anti-TB treatment may be deferred until the acute hepatitis has resolved. In other cases where TB treatment is needed during acute hepatitis, use a combination of four non-hepatotoxic drugs. Patients must continue follow-up by a specialist during TB treatment.

An asymptomatic increase in aspartate transaminase concentration occurs in approximately 20% of patients treated with the standard four-drug regimen; in most patients, asymptomatic aminotransferase elevations resolve spontaneously over days to weeks. Generally, majority of patients on TB treatment do not develop hepatotoxicity and it is not necessary to monitor liver function unless there is a clinical reason (such as history of prior liver disease or injury).

Risk factors for drug-induced liver injury include underlying liver disease (particularly hepatitis C) and co-administration of antiretroviral therapy for patients with HIV infection, especially with use of NNRTIs such as NVP.

The approach to management of hepatotoxicity associated with antituberculous drugs should be guided by liver function test results and the agent(s) most suspected of causing such results. In general, all hepatotoxic drugs should be discontinued if the serum bilirubin is ≥51 µmol/L or serum transaminases are more than five times the upper limit of normal. Once liver function tests return to baseline (or fall to less than twice normal), potentially hepatotoxic drugs can be restarted one at a time with careful monitoring between resumption of each agent. Close expert consultation with a physician or hepatic specialist or the National Program is advised if possible.

For further information on detection and management of hepatitis induced by anti-TB drugs, review Chapter 15 on Pharmacovigilance (section on adverse events associated with Anti-TB drugs).

6.6 TB and kidney disease

The term kidney disease reflects the entirety of acute kidney diseases and disorders and chronic kidney disease and can be defined further based on duration ie Acute kidney disease (duration ≤3 months) or Chronic kidney disease (duration >3 months). The risk of TB among patients with chronic renal disease risk is 6.9 to 52.5 times that of individuals without renal disease. Uremia causes reduced cellular immunity. Other factors that may diminish immunity in the setting of renal failure include malnutrition, vitamin D deficiency, and hyperparathyroidism.

Urogenital tuberculosis (TB) is the third most common form of extrapulmonary TB (after lymph node involvement and tuberculous pleural effusion). Complications of renal and urologic TB can lead to chronic kidney disease, especially in the setting of bilateral renal involvement and/or in the setting of interstitial nephritis or glomerulonephritis. Acute kidney disease can be further defined as follows:

- Acute kidney disease (AKD) – Acute Kidney Injury (AKI), or GFR <60 mL/min per 1.73 m^2, or markers of kidney damage for ≤3 months, or decrease in GFR by ≥35% or increase in serum creatinine by >50% for ≤3 months
- Acute kidney injury (AKI) – (subcategory of AKD) oliguria for >6 hours, rise in serum creatinine >0.3 mg/dL in 2 days or by >50% in 1 week

Chronic kidney disease (CKD) is defined as GFR <60 mL/min per 1.73 m^2 or markers of kidney damage for >3 months. CKD can be further classified on basis of Glomerular Filtration Rate as shown in the Figure 6.8 with the treatment options outlined.

Figure 6.8: Stages of Chronic Kidney Disease and Recommended Action Plan

Stage	*Description*	*Estimated GFR (mL per minute per 1.73 m²)*	*Action plan*
1	Kidney damage* with normal or increased GFR	≥ 90	Diagnose and treat chronic kidney disease and comorbid conditions, slow progression, reduce cardiovascular risk
2	Kidney damage* with mildly decreased GFR	60 to 89	Estimate progression
3a	Mildly to moderately decreased GFR	45 to 59	Evaluate and treat complications
3b	Moderately to severely decreased GFR	30 to 44	Evaluate and treat complications
4	Severely decreased GFR	15 to 29	Prepare for renal replacement therapy
5	Kidney failure	< 15 (or dialysis)	Renal replacement therapy if uremia present

GFR = glomerular filtration rate.

**—Markers of kidney damage are required for diagnosis of stage 1 or 2 chronic kidney disease.*

Adapted with permission from National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. *2002;39(2 suppl 1):S216, with additional information from references 21 and 23.*

Patients with CKD Stage 5 undergoing chronic dialysis are 6–52.5 times more likely to develop TB than the general population, mainly because of the impaired cellular immunity. Protein malnutrition, zinc and pyridoxine deficiency, and defects in leukocyte function following exposure to dialysis membranes increase the susceptibility of dialysis patients to TB.

Extra-pulmonary TB in patients on dialysis is more frequent (reported to be between 50% and 100%) with the most common forms of presentation being lymphadenitis, gastrointestinal, bone, genitourinary, peritonitis, pleural effusion, pericardial effusion, miliary TB, and pyrexia of unknown origin (PUO). TB in dialysis has a poor prognosis and high mortality mainly due to delay in diagnosis and adverse effects of anti-TB drugs. Therefore, a high index of suspicion for early TB diagnosis and treatment is required in patients on dialysis.

Patients with renal failure or severe renal insufficiency can receive the standard anti-TB regimens. Isoniazid and Rifampicin are eliminated by biliary excretion, so no change in dosing is necessary. There is significant renal excretion of ethambutol and metabolites of pyrazinamide, and doses should therefore be adjusted. Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg). While receiving isoniazid, patients with severe renal insufficiency or failure should also be given pyridoxine in order to prevent peripheral neuropathy.

Treatment of TB in dialysis is difficult and challenging. There is a high incidence of side effects from anti-TB drugs, especially neuropsychiatric, hepatic, and gastrointestinal. For patients on hemodialysis, administration of Ethambutol and Pyrazinamide should be done immediately after hemodialysis to facilitate directly observed therapy and minimize premature removal of the drugs.

Generally, it is not necessary to monitor renal or liver function, or blood counts unless there are clinical reasons to do so (e.g. a history of prior renal disease or injury or co-morbid diseases that may affect the kidney such as HIV or hypertension). The patient

should be reviewed by the renal specialist regularly in the renal unit while undergoing TB follow-up at the TB clinic. The patient undergoing dialysis should use appropriate IPC methods while in the dialysis unit.

Patients with renal insufficiency may have additional clinical conditions (such as diabetes with associated gastroparesis) that may affect the absorption of antituberculous drugs or may be taking other medications that interact with antituberculous drugs. Therefore, careful clinical and pharmacological assessment is required.

6.7 TB in pregnancy and lactation

6.7.1 TB and pregnancy

Pregnancy has not been shown definitively to influence the pathogenesis of TB or the likelihood of progression from latent infection to active disease, nor has it been shown to affect the response to treatment. 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.

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 of 2RHZE/4RH. These anti-TBs are not dangerous in pregnancy and are compatible with breastfeeding. Active TB in pregnancy is associated with adverse maternal and fetal outcomes; untreated active TB represents a greater hazard to the mother and fetus than anti-TB therapy.

Pregnancy and the early postpartum period may confer increased risk for isoniazid-induced hepatotoxicity. Therefore, pregnant women and postpartum women within three months of delivery should have baseline liver function testing prior to initiation of treatment for active TB and monthly testing in follow-up. Additional evaluation includes testing for HIV and hepatitis B and C.

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.

6.7.2 TB 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.

NUTRITION ASSESSMENT, COUNSELING AND SUPPORT IN TB

7

7.1: Introduction

Evidence has shown important links between improved treatment outcomes and good nutrition. Adequate nutrition is necessary to maintain the immune system and optimize response to medical treatment and sustain healthy levels of physical activity. Good nutrition also supports optimal quality of life for people with TB. Nutrition interventions also help to optimize the benefits of anti TB as well as increase compliance with treatment regimens, both of which are essential for curing and preventing transmission of TB

7.1.1: Definition of terms

Term	Definition
Nutrition	Nutrition refers to the sum of all processes involved in taking in of nutrients, their assimilation and use for proper body functioning and maintenance of health. The successive stages include; ingestion, digestion, absorption, assimilation and excretion.
Malnutrition	Malnutrition refers to deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients. The term malnutrition covers 2 broad groups of conditions. One is 'undernutrition'—which includes stunting (low height for age), wasting (low weight for height), underweight (low weight for age) and micronutrient deficiencies or insufficiencies (a lack of important vitamins and minerals). The other is overweight, obesity and diet-related non communicable diseases (such as heart disease, stroke, diabetes, and cancer).
Nutrients	These are molecules in food that all organisms need to make energy, grow, develop and reproduce.
Categories of nutrients 1. Macronutrients	Carbohydrates Protein Lipids

2. Micronutrients	Vitamins A, B, C, D, E, K Minerals- Iron, zinc, selenium, calcium
3. Others	Fiber /Roughage Water: At least 8 glasses or 2 litres per day

Table 7.1: Composition of Food; 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

TEN FOOD GROUPS

1. **Grains, white roots and tubers, and plantains**
2. **Pulses (beans, peas and lentils)**
3. **Nuts and seeds**
4. **Dairy**
5. **Meat, poultry and fish**
6. **Eggs**
7. **Dark green leafy vegetables**
8. **Other vitamin A-rich fruits and vegetables**
9. **Other vegetables**
10. **Other fruits**

7.2 Components of a Healthy Diet

When planning a meal, it is important to consider the following basic principles. The food groups below will help you achieve good feeding practices

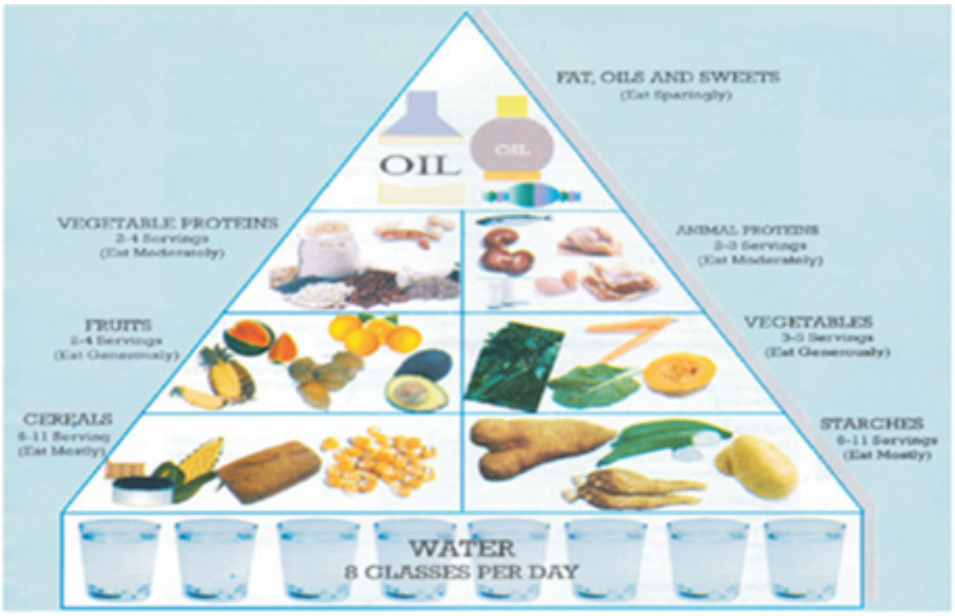


Figure 7.1: Food Pyramid Guide *(Source: Diabetes Educator, 2010)*

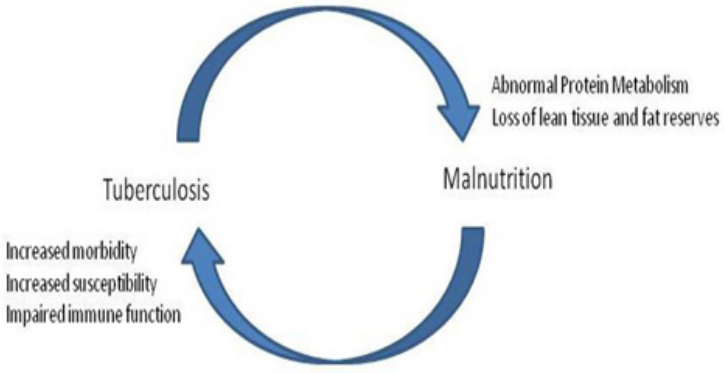
7.3 Relationship between Nutrition TB, Leprosy and Lung Disease

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.

7.4 Interaction between 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 7.2: Interaction between 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;

i) There's a 13% increase in basal metabolic rate (BMR) change with every 1-degree Celsius rise in body temperature

ii) The adipose and glycogen stores normally decrease due to increase in energy expenditure

iii) Loss of body fluids - sweating and urination during the acute phase hence electrolyte loss

iv) Loss of body weight due to increased catabolism

v) Reduced appetite and ability to take food (anorexia, Cachexia and generalized weakness

vi) Reduced ability of body to absorb nutrients

vii) Increased nutritional needs through metabolic changes

viii) Micronutrient deficiencies like zinc, vitamins A, C and D and iron

7.5 Role of nutrition in Tb, Leprosy and Lung Disease

Optimal Nutrition enhances:

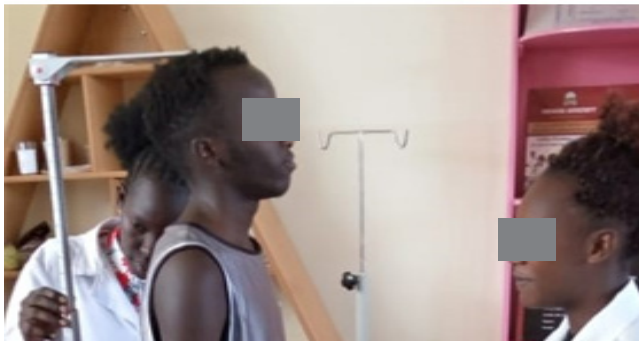
- Growth, development, replacement and repair of cells and tissues
- Helps chemical processes such as digestion, metabolism, assimilation and excretion
- Restores and protects the integrity of the immune system
- Prevent wasting and other forms of malnutrition micronutrient included
- Delay HIV progression
- Improve drug efficacy
- Optimize cellular activity and tissue/organ function by providing sufficient amounts that meets daily body requirements

7.6 Nutrition care process

There are four steps of nutrition care process

- Nutrition assessment
- Nutrition diagnosis
- Interventions
- Monitoring and evaluation

Nutrition assessment counseling and support (NACS)



Source: Kabarak University- Kenya 2019

KEY HIGHLIGHT

- All TB patients should receive nutritional assessment, counselling and support at baseline and monthly tailored to individual needs

7.7 Components of nutrition assessment, counseling and support

7.7.1: Nutrition assessment and diagnosis

Proper nutrition assessment (measurement and classification) is a prerequisite for provision of good nutritional care. NACS aims to establish routine nutrition assessment as an integral component of facility and community-based screening, care, and support. This can be interpreted by obtaining information from dietary, biochemical, anthropometric and clinical studies which are made up of surveys, surveillance or screening.

7.7.2 Aims of Nutrition assessment

i. Identify medical complications that affect nutritional status

ii. Track growth and weight trends

iii. Detect diet habits that make it difficult to improve health or that increase the risk of disease

iv. Inform nutrition messages and counseling

v. 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

7.8: Types of Nutrition Assessment

1. Anthropometric assessment
2. Biochemical assessment
3. Clinical assessment
4. Dietary assessment
5. Environmental assessment
6. Psychosocial assessment
7. Functional assessment

7.8.1 Anthropometric assessment

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 (refer to the SOPs)

7.8.2 Biochemical

These are chemical assays/ Lab assessments/analysis in most cases done on body fluids and have nutrition implications e.g. Hemoglobin, sugar levels, Liver function, CD4, Thyroid function, calcium levels, creatinine, kidney functions.

7.8.3 Clinical assessment

This involves physical observation/ judgement Signs of nutrient deficiencies like visible Wasting, hair changes, oedema, skin changes

Table 7.2: Clinical Assessment 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, B_2 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 pigmentation), 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

7.8.4 Dietary assessment

24-hour recall, food diary, food frequency and diet history

7.8.5 Environmental and psychosocial assessment

The environmental and psychosocial assessment will identify factors that might be supporting or weakening TB management. Assessment of a client's living environment should accompany the nutritional management. This includes assessment of:

- Personal hygiene and sanitation
- Housing environment
- Food handling practices that affect susceptibility to infection
- The client's perception of self and their ability to function in the community that contributes to nutrition outcome.

1. Strategies to improve sanitation and hygiene

- Always wash and rinse fresh fruits and vegetables or clean with mild disinfectants, and thoroughly rinse in clean running water
- Practice good hygiene, especially hand washing with soap and water at all critical times (for example, before preparing food, before eating, before feeding a baby, after visiting the toilet, after changing the baby's diapers).
- Store food appropriately to prevent contamination by bacteria and moulds.
- Avoid eating any food that may seem spoilt, for instance mouldy food or stale leftovers, even if they are reheated.

7.8.6 Functional

Functionality of body parts assess the energy levels- (ability to prepare or consume meals and mobility) lethargy and disability.

7.9 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.

At the nutrition diagnosis step documentation required includes; Anthropometric cut off points (z score/BMI for 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 months 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 months requires follow up

7.9.1 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.

7.9.2 Nutrition Diagnosis Component

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

7.9.3 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 7.3: Assessment Diagnosis and Classification of Malnutrition

CLASSIFICATION OF NUTRITIONAL STATUS AND MANAGEMENT

CHILDREN 6-59 MONTHS		
Weight/ Height Level	**Classification**	**Management**
80% or >-1z score or MUAC >=12.5	Normal	i) Nutrition counseling on weight maintenance ii) Vitamin A supplementation as per WHO recommendation iii) Monthly nutrition assessments
<80% or <-2z score or MUAC <12.5CM	Moderate acute malnutrition	i) Nutrition counselling on weight increase ii) Monthly nutrition assessments iii) Nutrition supplementation(Vitamin A, Fortified blended foods like fast food, Ready To Use Supplementary Food
<70% 0R -3 Z score or MUAC <11.5	Sever acute malnutrition without medical complication (passes appetite test, alertness, care giver willing to manage SAM at home	i. Nutrition counseling on weight increase ii. Weekly nutrition assessment iii. Therapeutic feeds (Ready To Use Therapeutic Foods either bar or Paste) per kg Bwt
<70% or -3 z score with oedema +++ or MUAC <11.5	Severe acute malnutrition with medical complication(fail appetite test, intractable vomiting, anorexia, high fever, convulsions, no alertness, lethargy, lower RTI, severe anemia or dehydration, hypoglycaemia and hypothermia)	Manage in inpatient set up as per IMAM guidelines

Table 7.4: BMI FOR AGE 5- 17 YEARS

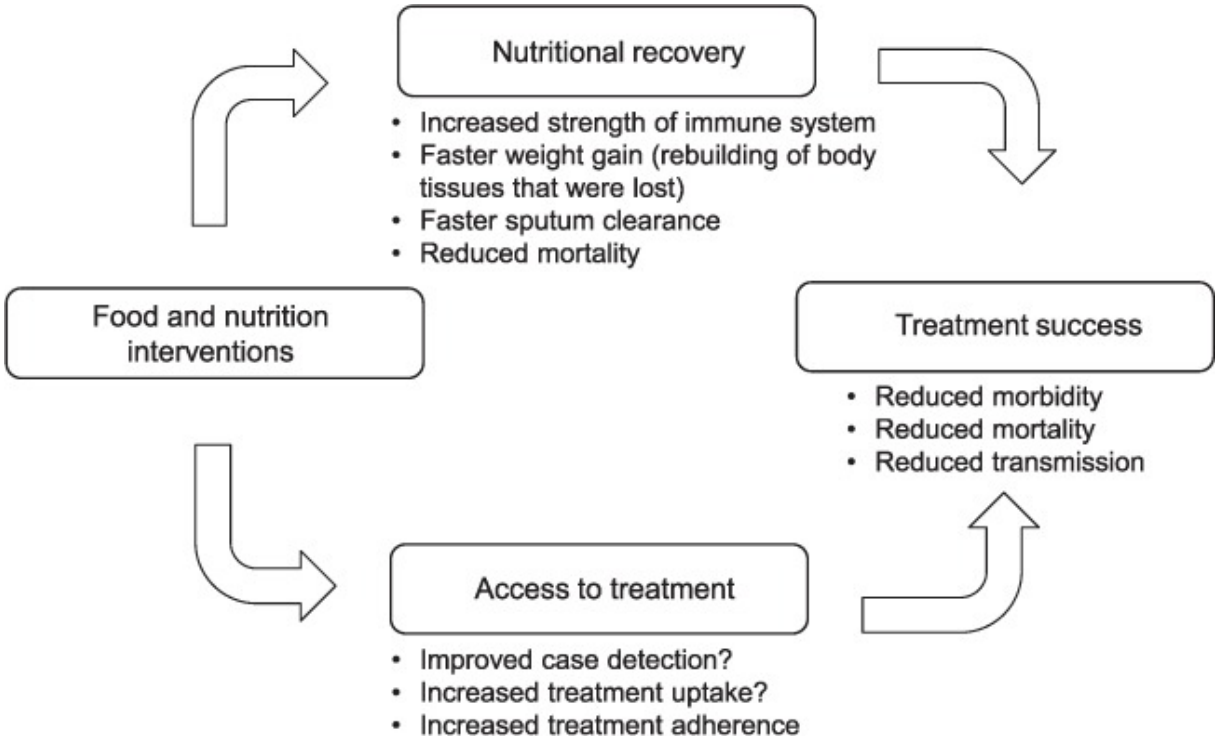
BMI FOR AGE	CLASSIFICATION	MANAGEMENT
80% or >-1z score or MUAC 5-9years >=14.5cm 10-14years >=18.5 15-17years >=19.5	Normal	Nutrition counseling on weight maintenance Vitamin A supplementation as per WHO recommendation Monthly nutrition assessments
<80% or <-2z score or MUAC 5-9years>=13.5 to <14.5cm 10-14years>=16 to< 18.5cm 15-17years>=17.5 to <19.5	Moderate acute malnutrition	Nutrition counseling on weight gain Monthly nutrition assessments Nutrition supplementation (Vitamin A, fortified blended flours, Ready To Use Supplementary Food
<70% 0R -3 Z score or MUAC 5-9years>=13.5cm 10-14years<16cm 15-17years17.5cm	Severe acute malnutrition without medical complication (passes appetite test, alertness, caregiver willing to manage SAM at home	Nutrition counseling on weight gain Weekly nutrition assessment Therapeutic feeds (Ready To Use Therapeutic Foods either bar or Paste) Hydrolysed feed for DRTB
<70% or -3 z score with oedema +++ or MUAC 5-9years<13.5cm 10-14years<16cm 15-17years17.5cm	Severe acute malnutrition with medical complication Fail appetite test(fail appetite test, intractable vomiting, anorexia,high fever, convulsions, no alertness, lethargy, lower RTI, severe anemia or dehydration, hypoglycaemia and hypothermia)	Manage in inpatient set up as per IMAM guidelines

Table 7.5 : BMI for Adults 18 Years and Above

BMI FOR AGE	CLASSIFICATION	MANAGEMENT
BMI >30	Obese	• Nutrition counselling on weight reduction and physical exercise • Vitamin A supplementation • Monthly nutrition assessment
BMI>25cm-29.9	Overweight	• Nutrition counselling on weight reduction and physical exercise • Vitamin A supplementation • Monthly nutrition assessment
BMI >=18.5-24.9 or **Pregnant and postpartum up to 6months MUAC= >23CM**	Normal	• Nutrition counselling on weight maintenance • Vitamin A supplementation as per WHO recommendation • Monthly nutrition assessments
BMI<18.5 or MUAC <23cm	Moderate acute malnutrition	• Nutrition counselling on weight increase • Monthly nutrition assessments • Nutrition supplementation(Vitamin A, Fortified blended foods like foundation plus, Read To Use Supplementary Food
BMI<16.5 CM or MUAC <19CM	Severe acute malnutrition without medical complication	• Nutrition counselling on weight • Weekly nutrition assessment • Therapeutic feeds (Ready to Use Therapeutic Foods either bar or Paste) • Hydrolysed feed for DRTB
BMI < 16.5CM with bilateral pitting oedema +++ or MUAC <16CM	Severe acute malnutrition with medical complication(fail appetite test, intractable vomiting, anorexia,high fever, convulsions, no alertness, lethargy, lower RTI, severe anemia or dehydration, hypoglycaemia and hypothermia)	• Manage in inpatient set up as per IMAM guidelines

For pregnant and postpartum mother	MUAC	>23	<23	<19	CLASS	Normal	MAM	SAM
	CLASS	Normal	MAM	SAM	MANAGEMENT	• NC and • IFAS	• RUTF and advantage plus • IFAS	

Figure 7.3: Cycle of Nutrition Interventions



Pathways through which food assistance can contribute to treatment success. Adapted from de Pee S, Grede N. Food and nutrition assistance in TB programming: rationale and practice. Symposium 'Action on the social determinants of tuberculosis: are social protection interventions 2012. http://tbsymposium.lshtm.ac.uk/files/2012/02/Nils-Grede.pdf Accessed May 2016

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.

7.10 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.

7.10.1 Nutrition Support

Nutrition support includes:

- Therapeutic and supplementary foods to treat clinical malnutrition.
- 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 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 hemoglobin level.

Water

Drink at least 8 glasses or more of safe water per day. This helps in preventing dehydration and flushing out toxins. (2litres)

Fiber

Low fiber diet is recommended as the patient nutrient intake is impaired. High fiber is likely to Keep the patient feeling full but of few calories.

i) Diet should be based on locally available foods

ii) Maintain a balanced diet with diversity

iii) The cost of the advised food should be affordable not catastrophic to the household

iv) Foods should be rich in all the essential Nutrients, carbohydrates proteins vitamins and minerals

v) The food should be appetizing and easy to ingest and digest

vi) Warm food often provides more appetite than cold food.

vii) Patients should eat enough food to maintain adequate nutrition.

viii) Avoid intoxicants and other harmful substances e.g. alcohol, cigarettes

7.11 Nutrition in special conditions

7.11.1 Nutrition Management of TB in Pregnant and Lactating Women

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 lactation, women are advised to consume an 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 7.6: 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 trimester 0-12 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.

7.11.2 Nutritional Management of Children

a) 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 TB Preventive Therapy (TPT) for high risk children who have no sign or symptoms of TB disease (Refer to LTBI).

b) 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.

c) 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 to 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 guidelines Kenya 2014, Egypt, TB 2007)

NOTE

Breastfeeding should be given on demand and mothers supported to exclusively breastfeed for 6months with a continuation to 24months. Babies staying away from their mothers should be fed on Expressed breast milk.

d) 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

7.11.3 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

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 intake 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.

Adequate micronutrient intake is best achieved through an adequate diet. However, in settings where these intakes and status cannot be achieved, multiple micronutrient supplements may be needed within the recommended RDA

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.

7.11.4 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 comorbidity experience delayed recovery of body mass and hemoglobin, 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 the 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 the 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

7.11.5: Nutritional management of patients with other comorbidities

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. Comorbidity with 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.

Food drug interaction

Table 7.7: Side Effects Related to TB Drugs and Food Intake and Recommendations to Minimize (Refer to PV)

DRUG RESISTANT TUBERCULOSIS (DRTB)

8

8.1. Introduction to DRTB

Drug resistant tuberculosis (DR TB) remains a major public health concern globally. The Global Surveillance data 2018 estimated 558,000 cases with MDR/RR TB and death rate of 240 000 cases and a treatment success rate (TSR) of 56%.

Kenya is among the highly burdened countries with TB, MDR TB and TB-HIV with an estimate of 1.3% among new TB cases and 4.4% of previously treated TB cases. In 2019, 692 DRTB cases were notified, an increase from 577 notified in 2018 attributed to improved DRTB surveillance that continues to expand through increased molecular access to molecular diagnostic testing. In 2019, 60% of the new cases and 79% of the previously treated cases received a Drug Susceptibility Test (DST) with Gene Expert, Culture and Line probe Assay.

8.2. Basic Concept(s) on Drug Resistance Development

The cause of Drug-resistance 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 three principal pathways of drug resistance development as outlined in the Table 8.1:

- **Injectable free regimen (IFR): This is a fully oral regimen recommended for MDR/RR and Pre-XDR (resistant to SLIs) TB patients including adults, children and pregnant women.**
- **New WHO Classification for second line drugs used in the treatment for DRTB**
- **Treatment of DRTB in special conditions (children, HIV, pregnancy and lactation, DM, Psychiatric and mental disorders, drug and substance abuse, DRTB contacts and renal disease)**
- **Use of PHQ-9 and CAGE 9 forms for the assessment of psychiatric and mental disorders in TB**
- **Post treatment follow up for DRTB patients**

Table 8.1: Pathways of Drug-Resistant TB development

1.Natural Resistance	2.Primary Resistance	3.Acquired Drug Resistance
- Occurs when all live species reach a certain number of divisions -They undergo random genomic mutations giving rise to organisms with certain altered functions	-A patient is infected with a resistant strain of the bacilli.	-Due to inadequate therapies leading to selection of mutant resistant strains-it's an expression of poor treatment

8.2.1: Factors associated with Drug-Resistant TB Development

There are several factors associated with DRTB development. These can be classified in to three, namely:

1. Health care-related factors

2. Drugs –related factors

3. Patient related factors

The table below describes each in details.

Table 8.2. Factors associated with Drug-Resistant TB Development

Healthcare factors	Drugs related factors	Patient-related factors
• Non-compliance to guidelines • Inadequate training • Poor treatment monitoring • Poorly organized or funded TB control programs	• Inadequate supplies • Poor quality • Poor storage conditions • Wrong dose or combinations • Poor regulation of medicines • Unavailability of certain medicines	• Poor adherence or poor DOT • Lack of information • Lack of transportation • Adverse effects • Social barriers • Malabsorption

8.3: Classification of Drug-Resistant TB

Classification of DRTB is as described in the tables below:

1. Classification based on the Resistance patterns after drug susceptibility testing.

Table 8.3: Classification based on the Resistance pattern:

Resistance pattern	Definition
Presumptive drug-resistant TB case	These are Individuals with a higher risk of getting drug resistant 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 the known MDR-TB patient, refugees, prisoners, health care workers with symptoms of TB, DR TB contacts.
Monoresistance	Resistance to one first-line anti-TB medicine only.
Poly-drug resistance (PDR)	Resistance to more than one first-line anti-TB medicine (other than both Isoniazid and Rifampicin)
Multi-drug resistance (MDR)	Resistance to at least both Isoniazid and Rifampicin
Rifampicin resistance(RR)	Resistance to Rifampicin detected using phenotypic or genotypic methods, with or without other anti-TB drugs. It includes any resistance to Rifampicin, whether mono resistance, multidrug resistance, Poly-drug resistance or extensive drug resistance.
Isoniazid resistance	Refers to Mycobacterium tuberculosis strains with resistance to isoniazid and susceptibility to rifampicin confirmed in vitro
Pre-XDR	Resistance to Isoniazid and Rifampicin and either a fluoroquinolone or a second-line injectable agent but not both.
Extensive drug resistance (XDR)	Resistance to any Fluoroquinolone and at least one of three second-line injectable drugs (Capreomycin, Kanamycin and Amikacin), in addition to multidrug resistance.

2. Classification based on the registration group:

Table 8.4: Classification based on the registration of DR TB patients

Registration group	Definition
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 second-line regimen because of resistance are placed in this group, even if they received more than one month of Category I treatment).

Registration group	Definition
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 the failure of First-Line Treatment (FFT)	Patients who return after having failed the first treatment i.e smear-positive at earliest, month 5
After the failure of Retreatment (FRT).	Patients who return after having failed the re-treatment.

3. Classification based on the anatomical pathological site of the lesion either within or outside the lung parenchyma as described in the table below.

Table 8.5: Classification based on the Anatomical site

Classification	Definition
Pulmonary Drug resistant TB	Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. This exclude pleural effusion -Milliary TB is classified as PTB because the lesions are in the lungs. -Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra pulmonary TB. -**A patient with both pulmonary and extra pulmonary TB should be classified as a case of PTB**
Extra pulmonary Drug Resistant TB	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.

4. Classification based on the status of HIV infection: all TB diagnosed patients should have an HIV test done and documented.

Table 8.6: 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 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 re-classified 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

8.4: Diagnosis of Drug Resistant TB

The approach to diagnosis begins by identifying the high DR TB suspects or the individuals at high risk of developing DRTB and obtaining relevant samples for Mycobacteriological testing.

People at high risk for DR TB include:

1. DR TB contacts with symptoms of TB. Includes children with TB symptoms who are contacts of DR TB source persons.
2. Failures on Drug susceptible TB treatment (smear positive at month 2 and 5)
3. Patients who develop TB while on IPT
4. Health care workers with TB symptoms.
5. Refugees with TB symptoms
6. Prisoners with TB symptoms
7. All previously treated patients. They include, failures, relapses, return after loss to follow ups.

The definitive diagnosis of drug-resistant TB requires the detection of Mycobacterium tuberculosis bacteria and determination of resistance to anti-TB drugs using the methods outlined below:

a) Genotypic:

These include:

- **Gene Xpert**

It's an instrument used to rapidly diagnose Mycobacterium Tuberculosis and determination of Rifampicin resistance.

It is preferred as the first test for TB diagnosis and identification of Rifampicin Resistance for all presumptive TB cases. It has a sensitivity of 96% and specificity of 98%.

Its limitations and strengths are outlined in the Table 8.7.

Table 8.7: Strengths and limitations for Gene Xpert testing

Strengths	Limitations
• Increased sensitivity • Detection of Rifampicin-resistance pattern • Reduced turnaround time • Requires minimal skills and infrastructure	• It is **NOT** recommended for patient monitoring treatment (it detects both live and dead bacilli) • It may result in discordance with phenotypic DST results. (GeneXpert covers 95% of the gene region) • Limited ability to detect Mixtures of susceptible and resistant TB

- **Line Probe Assay(LPA)**

The techniques share the same fundamental principles as GeneXpert. They are both PCR based.

This technique is used to detect Mycobacterium Tuberculosis Complex (MTC) as well as drug sensitivity to 1st line drugs (Rifampicin and Isoniazid) and 2nd line drugs (Fluoroquinolones and 2nd line injectable drugs).

The strengths and limitations for Line Probe assay is outlined in the table below.

Table 8.8: Strengths and limitations for Line Probe Assay

Strengths	Limitations
• LPA produces results in just 24-48 hours. • It allows quick triage of confirmed rifampicin-resistant or MDR-TB patients into either the shorter MDR-TB regimen or the conventional longer regimen	• It requires adequate and appropriate laboratory infrastructure and equipment. • It requires adequate and skilled laboratory staff

b) Phenotypic:

1. Culture

It is the gold standard for TB diagnosis and can detect as few as 10-100 live bacteria/ml.

Examples:

1. Liquid Culture-Mycobacterium Growth Indicator Tube (MGIT)

2. Solid Culture-Lowenstein-Jensen (LJ)

Culture and drug susceptibility testing is indicated for all bacteriological diagnosed TB cases.

Strengths	Limitations
• Requires as few as 10 bacilli/ml to detect TB • Allows drug susceptibility testing and DR surveillance	• The slow growth of MTB thus delayed turn-around-time • Requires huge infrastructural capacity to set up

2. Drug Susceptibility Testing (DST)

A laboratory method that determines whether bacteria will grow in the presence of TB drugs. If bacterial growth is observed, that indicates resistance, while no growth indicates susceptibility to TB drugs used.

Indications for DST	
First Line DST • Previously treated patients; • Persons who develop active TB after exposure to a patient with documented DR-TB • Patients who remain smear-positive at month two and five of therapy	**Second Line DST** • Patients with a DST showing resistance to at least rifampicin, isoniazid or both rifampicin and isoniazid at baseline • Patients who remain culture-positive on or after Month 3 DR TB. • Persons who develop active TB after exposure to a patient with documented DR-TB

8.5: Treatment

Treatment and care for DRTB has been decentralized in Kenya's 47 counties and 300 sub-counties. The implementation of the programmatic management of drug resistant TB (PMDT) began in 2006 with injectable agents as core medicines in the treatment regimens and has rapidly evolved ever since based on WHO guidelines.

In 2018, the World Health Organization (WHO) recommended the use of injectable free regimens (IFR) for the treatment of drug-resistant TB following new evidence that the new molecules (**Bedaquiline** and **Delamanid**) and repurposed drugs (**Linezolid** and **Clofazimine**) were **safer** and **more efficacious** compared to the injectable medicines, and Kenya transitioned on **1st January 2020** following a rapid communication on the same.

8.5.1 Principles and rationale for DR TB treatment

The treatment of DRTB is based on the following principles and rationale:

- Drug combinations should be used for TB/DR TB treatment. This prevents the appearance of resistance as it avoids the selection of naturally occurring resistant mutants.

- Intentional or inadvertent monotherapies should NEVER be used for it may result in the high possibility to select naturally occurring mutants to the single drugs used. It is important to note that anti TB medicines do not select the resistant mutants, as they do not cause mutations.
- The regimen composition should have drugs with Sterilizing and Bactericidal effects.
- Treatment should be long enough to permit action against all bacillary populations.

8.5.2 Treatment objectives:

They include:

1. To rapidly reduce the patient's risk of death, symptomatology and their infectiousness
2. To cure without relapses
3. To avoid selection of resistance by using an adequate number of drugs for each treatment phase.

8.5.3 Classification of anti TB drugs used in the management of DR-TB

The 2019 WHO classification of anti-TB drugs used in the management of DR-TB is based on their efficacy and experience for use as described in the table below.

Table 8.9: Grouping Medicines for use in the treatment of drug-resistant TB

Group	Medicine	Abbreviation
Group A Include all three medicines (Unless the cannot be used)	Levofloxacin or Moxifloxacin	Lfx Mfx
	Bedaquiline	Bdq
	Linezolid	Lzd
Group B Add both medicines (Unless they cannot be used)	Clofazimine	Cfz
	Cycloserine or Terizidone	Cs Trd

Group C Add to complete the regimen and when medicines from Group A and B cannot be used	Ethambutol	E
	Delamanid	Dlm
	Pyrazinamide	Z
	Imipenem/Cilastatin or Meropenem	Imp/Cln Mpn
	Amikacin or (Streptomycin)	Am (s)
	Ethionamide or Prothionamide	Eto Pto
	p-amino salicylic acid	PAS

NOTE

- **This new classification is intended to guide the design of longer individualized regimens; however, majority of DRTB patients will be on standardized regimens.**
- **Medicines in Group A and C are shown in decreasing order of usual preference for use (most preferred comes first)**
- **Always use Carbapenems e.g. Imipenem/Cilastatin together with Clavulanate**
- **Group C drugs should only be added to complete the regimen and when medicines from Group A and B cannot be used.**

8.5.4 Treatment regimens by resistant patterns

The Injectable free treatment regimen:

It is the recommended regimen for MDR/RR and Pre-XDR (resistant to SLIs) TB patients including adults, children and pregnant women. The Drugs used in these regimens are administered orally.

This regimen has two phases:

1. **Intensive phase:** 6 months

The end of intensive phase is defined by a negative culture at the end of the 3rd month and three consecutive negative smears taken 30 days apart after month 3. This phase may be extended in **consultation** with the National PMDT to 7 and/or 8 months in any of the following situations

a) Slow clinical response to treatment after clinical evaluation, characterized by:
   i. Ongoing /worsening TB (pulmonary) symptoms (cough, fever, drenching night sweats and weight loss/poor weight gain)
   ii. Worsening radiological features i.e. cavities, infiltrates, opacities

b) Delayed smear or culture conversion

c) Cases where baseline SL LPA results are indeterminate/FLQ susceptibility is not confirmed.

A negative culture at month 4 and negative smears at the end of month 7and/or 8 month marks the END of the extended intensive phase and **should not** be extended further.

2. Continuation phase: 12 months

The continuation phase starts from month 7 as determined by culture/smear results or at the end of the extended intensive phase where applicable. The continuation phase is 12 – 14 months depending on the DST pattern. Reversion of sputum cultures (from negative to positive) indicates treatment failure. In case of reversion, a multi-disciplinary team should urgently review the patient and the national clinical team informed as soon as possible.

The following should be reported to the National Clinical Team;

- Any person with DRTB who is not eligible for the standardized regimens due to previous history of DRTB treatment
- Any person with DRTB requiring modification of regimen in the continuation phase e.g. use of both Bedaquiline, Delamanid and linezolid in the continuation phase
- Any person with DRTB who has any contraindication or toxicity to one of the five core drugs in the intensive phase thus requiring an individualized regimen
- Any person with DRTB who has Hb<8g/dl, neutrophils <0.75x10^9/L or platelets <50 x10^9/L during treatment while on linezolid

The table below describes the treatment of DRTB according to the resistant patterns

Table 8.10: Kenya DR-TB treatment regimens according to resistant patterns

Pattern of Drug Resistance	Regimen	Duration
MDR/ RR TB	**Intensive phase: 6 Bdq/Cfz/Lfx/Cs/Lzd** **Continuation phase: 12 Cfz/Lfx/Cs**	18 months
Pediatric MDR / RR TB (<6yrs and <25kg)	**Intensive phase: 6 Mfx/Cfz/Cs/Lzd** **Continuation phase: 12 Mfx/Cfz/Cs**	18 months
Pre-XDR - Injectable resistant	**Intensive phase: 6 Bdq/Cfz/Lfx/Cs/Lzd** **Continuation phase: 12 Cfz/Lfx/Cs/**	18 months
Pre-XDR - Fluoroquinolones Resistant	**Intensive phase: 6Bdq/Dlm/Lzd/Cfz/Cs/** **Continuation phase: 14 Dlm/Cfz/Cs**	20 months

Pattern of Drug Resistance	Regimen	Duration
Pre - XDR Pediatrics'* - Fluoro-quinolone Resistance	**Intensive Phase:** **6 Bdq**/*Dlm/Lzd/Cfz/Cs** **Continuation phase: 14 Dlm/Cfz/Cs/Z**	20 months
ISONIAZID mono resistance	**6 RZE/Lfx** **(with pyridoxine)**	6 months
Bedaquiline Intolerance (In cases of Severe Adverse Events or hypersensitivity)	**Intensive Phase: 6 Dlm/Lzd/Lfx/Cfz/Cs** **Continuation phase: 12 Lfx/Cfz/Cs**	18 months
Poly-drug resistance (PDR TB) (HE/HEZ +-S)	**9 RZE/Lfx** **(with pyridoxine)**	9 Months
Pyrazinamide mono-resistance(Z) Or Pyrazinamide and Ethambutol (EZ) without INH resistance Or Ethambutol Mono-resistance(E)	**2 RHZE** **4 RH** **(with pyridoxine)**	6 months
Extensively Drug-resistance (XDR)	**Individualized regimen**	18-24 months
Any case excluded from any of the regimens above	**Individualized regimen**	18-24 months

**Delamanid should only be prescribed in children under 3 years after consultation with the National Clinical team*

***Bedaquiline use in Paediatrics requires dissolution in water*

The construction of individualized regimens should be in consultation with the National clinical review team

8.5.6: Dosing schedules for DRTB treatment

Table 8.11 describes the dosing schedules for DRTB treatment in adults and adolescent patients.

Table 8.11: Adult & Adolescent dosing schedules

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
*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
Clofazimine 100mg	100 mg			
Bedaquiline	400mg daily for 2 weeks followed by 200mg three times/week (Monday, Wednesday and Friday) for 22 weeks			
Delamanid	100mg twice daily for 24 weeks	100mg twice daily		
Linezolid	Reduce to 300mg if severe ADR	300mg daily	600mg daily	
Pyridoxine (50mg)	For every 250 mg of Cycloserine, give 50 mg of Pyridoxine. Maximum dose of 200 mg			

**Kanamycin may be dosed three times per week (TIW) for months 5-6 week of the shortened DRTB regimen and for the full duration of intensive phase in longer individualized DR TB regimens including Pre-XDR and XDR TB.*

***If a higher dose of Moxifloxacin 800mg is not tolerated reduce to 400mg*

Table 8.12: Paediatric Dosing schedule

Drug name	Daily paediatric dose in mg/kg (maximum dose in mg)
Amoxicillin-Clavulanate	80 mg/kg (4000 mg amoxicillin and 500 mg Clavulanate): only to be given with Meropenem
Clofazimine	2 – 3 mg/kg
Delamanid	50 mg twice daily for 20 to 34 kg, for 6 months 100 mg twice daily for > 35 kg, for 6 months
Ethambutol	15 – 20 mg/kg (1000 mg) twice a day
Isoniazid	15 – 20 mg/kg
Levofloxacin	15 – 20 mg/kg (1000 mg)
Linezolid	10 mg/kg/dose twice daily
Meropenem	20 – 40 mg/kg (6000 mg)
Moxifloxacin	7.5 – 10 mg/kg (800 mg)
PAS	200 – 300 mg/kg
Pyrazinamide	30 – 40 mg/kg
Terizidone	10 -20 mg/kg (1000 mg) twice a day

8.5.7 Treatment Delivery models in Kenya:

There models of DRTB care and treatment and the criteria for selecting each care models is dependent on the following factors:

1. Clinical status and the general condition of the patient
2. The geographical location / terrain and ease for accessibility
3. The distance between the patient's home and the nearest health facility
4. Mental status of the patient
5. Patient's preference
6. Social dynamics surrounding the patient.

Below is a detailed description on the criteria for selecting a DRTB treatment / care model

Isolation	**Facility-based(ambulatory)**	**Community-based**
Preferred for **-** Severely ill patients - Patients with poor adherence - Refugees, street families and the homeless - Mobile populations - Patients with Total Drug resistance - Patients with mental illness without family support	**Preferred when** - Patient chooses to receive care in the health facility - Access to a health facility with access to transport - Stable General condition of the patient.	**Preferred for** - Patient choice to receive care while in the community - Confirmed treatment supporter - Transport challenges to access a health facility - Stable general condition.

8.5.8: DR TB Clinical teams' composition and their roles

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 following:

1. County TB coordinator,
2. The clinician (Physician/MO),
3. Sub-county TB coordinator,
4. Pharmacist, DOT Nurse,
5. Social worker,
6. Public health officer,
7. Lab technologist,
8. Nutritionist,
9. Community Health Extension Worker.

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

8.5.9 Patient workup

After the diagnosis of DRTB, pre-treatment preparation, evaluation, investigations and procedures should be done before initiating treatment. This is aimed at boosting compliance and adherence to the already complex DRTB treatment and prevent negative outcomes.

1. **Pretreatment evaluation**

- Confirm diagnosis of DR TB

  Note: DR-TB is a laboratory diagnosis (except in child contacts of DR TB who are unable to expectorate) hence every effort should be made to obtain a specimen and conduct (drug susceptibility testing) DST.

- Inform the patient of the diagnosis
- Educate and counsel the patient on DR TB, its treatment, need for adherence and DR TB models of care.
- Obtain a thorough history and perform a physical examination
- Obtain an informed treatment consent for treatment
- Conduct a home visit and contact screening
- Baseline ECG, Visual acuity testing, Neuropathy screening
- Baseline lab tests
- Establish a PMDT team to guide clinical management/ follow-up

NOTE:

Efforts should be geared towards meeting all the above conditions before treatment initiation. However, failure to meet the above conditions should not be a reason to delay treatment initiation.

2. **History taking**

What history should be taken from DR TB patients?

- Demographic Data/ Patient bio data
- TB History on: Date of previous diagnosis, type of TB start and end dates of treatment, history of HIV co-infection, Microscopy, culture and DST results, Adverse effects & complications

- Past Medical and social History with focus on: LMP & method of contraception, Prior comorbidities, history of medication, Alcohol, drug & tobacco use, drug allergies
- DR TB Contacts: Identify contacts, line list in the contact management register, screen using Chest X-ray and symptoms screening and test all presumptive DR TB using GeneXpert. Conduct home visits to screen contacts and assess TB IPC measures

3. Physical Examination

On examination, the clinicians should elicit the following

1. Vital signs: Blood pressure, Temperature, Pulse, respiration and Oxygen Saturation (SpO_2)
2. Anthropometric measurements: BMI and Z-scores
3. General and Systemic examination
    - All body systems should be examined, not just the respiratory system
    - Visual acuity tests (Ishihara charts and Snellen's charts) and neuropathy screening should be done for all patients.

4. Review of systems for the suggestion of advanced disease
    - Fever
    - Extra pulmonary signs e.g. CNS signs, effusions
    - Respiratory distress
    - Cachexia (extreme weight loss)

4. Laboratory, radiological and clinical investigations

i. Radiological

- Chest X Ray (Chest CT for patients with access)
- Any other radiological test as necessary for extra-pulmonary DR TB e.g. Head CT scan for patients with CNS signs

ii. Bacteriological Investigations

- Sputum for Smear microscopy
- Culture / DST and LPA for first and second Line drugs

iii. Laboratory investigations Lancet request forms.pdf

- HIV test for all patients
- Biochemistry: Urea, Creatinine, Electrolytes, ALT/AST/Bilirubin, Serum Albumin, RBS (FBS/HbA1c may be done if accessible)

- TSH
- Haemogram
- For women of childbearing age do a pregnancy test

iv. ECG

v. **Audiometry (hearing test) if injectable drugs are to be used.**

4. Patient Education and Counselling

Counselling for DRTB patients is important. It is aimed at identifying underlying psychosocial issues that would affect treatment delivery. The table below is a detailed description of counselling sessions and the content covered in the course of treatment.

Table 8.13: DRTB counseling sessions

Phase	Session	Content
At Baseline	First contact with the patient (Provide a session at the time of giving results)	• Establish rapport and assuring confidentiality • Introduction to DR TB and clinical team • Educate patients on TB treatment and prevention; transmission, common drugs side effects • Patients assessment - social and mental (refer details in the tools) • Family planning and contraception including testing-HIV and Pregnancy. • Roles and responsibilities for the patients, family, patient supporter and health care worker • The signing of the consent form
Intensive phase	At week 2	• Adherence, supportive education • Mental health assessment - Patient Health Questionnaire 9 (PHQ 9) • Psychosocial review and support • Side effect monitoring
	If major issues are identified, intensify adherence session (every 2 weekly)	• Adherence, supportive education • Mental health assessment • Psychosocial review and support • Side effect monitoring • Flag file for clinical team awareness

Phase	Session	Content
	If NO major issue identified, see the patient on monthly basis	• Adherence, supportive education • Mental health assessment • Psychosocial review and support • Side effect monitoring
Continuation phase: follow-up	Once a month, until completion of treatment	• Adherence: support and education • Mental health assessment • Side effects monitoring • Preparation for reintegration to community • Emotional validation, reassurance about regaining functionality (at work, sexual life etc.) • Family planning and contraception

NOTE:

1. **Patients may have a positive smear with a negative culture. That may be caused by the presence of dead bacilli and hence does not necessarily indicate treatment failure.**
   Action: DISCUSS such cases with the Sub-county and County DR TB Clinical teams.
2. **In patients with repeated negative culture and smear results with no corresponding clinical and radiological improvement.**
   Action: County or Sub County clinical team to evaluate for other conditions.
3. **Children with high clinical suspicion of TB should be treated for TB (empirically with the same regimen as the source contact) even if the result is negative.**

The Patient Health Questionnaire -9 (PHQ-9)

The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring and measuring the severity of depression.

This easy to use patient questionnaire is a self-administered version of the PRIME-MD diagnostic instrument for common mental disorders.

It is not a screening tool for depression but it is used to monitor the severity of depression and response to treatment. However, it can be used to make a tentative diagnosis of depression in at-risk populations.

The PHQ-9 score is obtained by adding scores for each question (total points).

An image of the PHQ-9 form and interpretation is shown below.

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ **DATE:**_____

Over the last *2 weeks,* how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
		add columns	+	+

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems,* how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all _____ Somewhat difficult _____ Very difficult _____ Extremely difficult _____

Interpretation

Provisional Diagnosis and Proposed Treatment Actions		
PHQ-9 Score	**Depression Severity**	**Proposed Treatment Actions**
0 – 4	None-minimal	None
5 – 9	Mild	Watchful waiting; repeat PHQ-9 at follow-up
10 – 14	Moderate	Treatment plan, considering counseling, follow-up and/or pharmacotherapy
15 – 19	Moderately Severe	Active treatment with pharmacotherapy and/or psychotherapy
20 – 27	Severe	Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

- Total scores of 5, 10, 15, and 20 represent cut points for mild, moderate, moderately severe and severe depression, respectively.
- Note: Question 9 is a single screening question on suicide risk. A patient who answers yes to question 9 needs further assessment for suicide risk by an individual who is competent to assess this risk.

8.6: DR TB in Special Situations

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

Sub-County TB Coordinators must be informed about these cases and further guidance sought from the National PMDT COE. Reference should be made to 2020 National PMDT Guidelines for detailed management of each case.

The table below is a summarized guide on the management of DRTB in special conditions.

Table 8.13: Treatment for DR TB in Special Conditions

Special population	Comments / recommendations
HIV	- Bdq cannot be used with EFV containing regimen (EFV reduces Bdq levels in the blood). Optimize ART regimen with Dolutegravir (DTG). - Monitor for other potential additives/overlapping toxicities for ART and Anti TB's. - Avoid Lzd if Hb<8 with pancytopenia - Give preference to TB treatment in TB and HIV Co-infection. Initiate ART treatment within 2-8 weeks. - Monitor for IRIS (Immune Reconstitution Inflammatory Syndrome) and manage according to ART guidelines.

Special population	Comments / recommendations
Children	- Moxifloxacin is preferred for use in pediatric DR TB regimens over levofloxacin because of its superior bactericidal and sterilizing activity and is well tolerated in most instances. - Children who are contacts of DR TB should be treated as the Index case (the person who is likely to have infected the child) - Treatment should be initiated even without Lab confirmation (Empirically using the DST of the index case) - **Use of Quinolones is permitted as benefits outweigh the risks.** - The duration of treatment is the same as for adults. - Dosing should be weight based
Pregnancy and Lactation	- Pregnancy is not a contraindication for treatment of active drug-resistant TB - Consider drug safety profiles. Avoid class D drugs (aminoglycosides). - Lactation is permitted. However, limit time of contact with the child to prevent the spread of infection. - Nausea and vomiting may be additive, observe and monitor for severity and manage accordingly. - **Linezolid, Bedaquiline, Clofazimine and Delamanid can be used safely.**
Diabetes Mellitus	- Monitor blood sugars closely (glycemic controls). - Educate patients on diet, treatment compliance, and lifestyle modification. - Monitor for renal insufficiency, neuropathy and screen for visual impairment - Refer to DM care clinics.
Renal disease	- Monitor and correct electrolyte impairment *(ref. to table on electrolyte replacement-side effects)* - Refer for specialized care
Liver disorders	- Monitor closely for liver function tests - Closely monitor for potential hepatotoxic drugs (pyrazinamide, isoniazid, fluoroquinolones, Bedaquiline) -Refer for specialized care.
Psychiatric / mental disorders	- Screen for depression and mental illness using the **PHQ9 form**. - Cycloserine deserves close monitoring as it may worsen the symptoms (use adequate effective dosages). - Refer for specialized care.
Drug and substance dependence	- Screen using CAGE 9 - May require admission and specialized inpatient care (isolation house/ward).

Special population	Comments / recommendations
DR TB contacts	-Trace, screen and investigate using CXR and GXP testing for those who are symptomatic. -Those diagnosed with active disease should be treated as the index case (inform County and Sub-County clinical teams). -Offer IPC messages -Invitation and symptom screening in the course of treatment for index cases every 3 months.

8.7 DR TB Treatment Monitoring and Follow up

Treatment monitoring and ensuring the delivery of quality healthcare is critical in DR TB management given the myriad of challenges associated with it.

Rationale

Patients on DR-TB treatment need to be monitored for treatment response or failure and safety, using reasonable schedules of relevant clinical, radiological and laboratory testing. Response to treatment and toxicity is monitored through regular history taking, physical examination, chest radiography, special tests such as audiometry, visual acuity tests, electrocardiography and laboratory monitoring.

Table 8.14: The role of health care givers in the delivery of quality of care

Cadre	Role in monitoring and recommended frequency
Clinician	- Review patients every day if hospitalized and at least every week if managed as an outpatient. - Conducts patient counseling, screening for substance abuse, ADR screening, monitor patient weight, height and BMI/ Z score at baseline and monthly thereafter until completion of treatment
	- Supervises daily intake of medication and signals any concerns to the clinician.
Multidisciplinary clinical review team (CRT)	- Physically reviews all DR TB patients within the sub-county at least once a month, and updates the clinical review checklist in the patient logbook - Document guidance to the clinician and DOTs provider on patient management for the next month in the patient logbook

8.7.1: Treatment monitoring and quality of care

Treatment monitoring refers to a systematic process of tracking patients through the whole continuum of care.

This process is aimed at ensuring adherence to treatment and management of adverse events with an aim of improving treatment outcomes.

Below is a description of monitoring schedule with parameters monitored and the frequency.

Table 8.15: Laboratory and other parameters monitored during DR TB treatment

Parameters Monitored	Frequency
Sputum smear and cultures	- Done at baseline and repeated every month until the end of treatment. - Microscopy is used for monitoring response to treatment while Culture is used to determine response and define cure.
Audiometry	- Done monthly if on an injectable drug. If any abnormality is detected, stop the injectable and refer for audio care. Repeat audiometry 3 and 6 months thereafter.
1st Line DST	- At baseline. This should also be done anytime there is a positive culture in a previously culture negative case.
2nd Line DST	- Done for all patients at baseline, month 3 and if a previously culture negative patient turns positive.
CXR	- At baseline and at the end of treatment
Full Haemogram	- At baseline, month 1 to 6 and monthly for every month the patient is on Linezolid
Serum Creatinine	- Done at baseline and monthly if on an injectable drug. Otherwise repeat only if the baseline creatinine was abnormal or if clinically indicated
Serum potassium, Magnesium	- Done at baseline and monthly if on an injectable drug. Otherwise repeat if vomiting, diarrhea, if QTcF is prolonged or if clinically indicated
TSH	- For patients on Prothionamide / PAS. Done at baseline and at month 2 if any abnormality was detected at baseline.
	- If hypothyroidism is present monitor monthly until treatment completion.
Serum Albumin	- Done at baseline for patients on Bedaquiline & Delamanid. Repeat as necessary
LFTs (AST, ALT, Bilirubin)	- Done at baseline. Repeat if patient is vomiting, abdominal pain, jaundice or any evidence of liver injury

Parameters Monitored	Frequency
HIV screening	- At baseline. Repeat at month 3, 6, 12 and 18 if negative
CD4	- At baseline. Repeat at month 6 and 12 if baseline CD4 was <200
Viral Load	- Done at 6 months then yearly.
Review of Contraception	- All women of childbearing age should be encouraged to use long-term contraception. This should be reviewed monthly.
Pregnancy test	- At baseline for women of child bearing age; repeat if indicated.
RBS	- At baseline, repeat if clinically indicated

NOTE:

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

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

8.8. DR TB Treatment Outcomes

8.8.1: 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 is 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

Treatment failed or **lack of conversion** by the end of the intensive phase implies that the patient did not convert within the maximum duration of the intensive phase. 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 purposes of defining Treatment failure, reversion is considered only when it occurs in the continuation phase.

8.9. DR TB Treatment failures

While treating MDR TB, some unfavorable 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 - 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:

- Review the treatment card and assess adherence to determine if the patient is receiving all the right drugs and doses.
- Review all DST reports to determine the adequacy of the regimen and consider an alternative regimen where possible.
- Repeat 1st and 2nd line DST to look for resistance amplification.
- A clinical management meeting should be convened urgently to discuss the patient.
- Look for other illnesses that may decrease absorption of medication (like chronic diarrhoea)

8.10: Adverse reactions and their management

Introduction

TB program systematically monitor patient safety to prevent and manage adverse drug reactions (ADRs), as well as improve health-related quality of life and treatment outcomes for patients who have TB. National tuberculosis programmes is actively pursuing drug safety monitoring and management to better preparedness to introduce new tuberculosis (TB) drugs and novel regimens.

Pharmacovigilance definition

The science and activities related to detection, assessment, understanding and prevention of adverse effects or any other possible medicine related problems. The Pharmacovigilance of importance in PMDT is active Drug safety monitoring for serious adverse drugs reactions.

Active TB Drug Safety Monitoring and Management (aDSM)

Active TB drug safety monitoring and management (aDSM) is defined as an active and systematic clinical and laboratory assessment of patients while on treatment (ref). aDSM applies to patients on treatment with: (i) new anti-TB drugs; (ii) novel MDR-TB regimens; or (iii) extensively drug-resistant TB (XDR-TB) regimens, in order to detect, manage and report suspected or confirmed drug toxicities. The recording and reporting of aDSM primarily targets common side effects and adverse drug reactions (ADRs) as a core requirement. Core components of aDSM include clinical monitoring, clinical management, recording and reporting.

Detection of ADRs and Adverse events

ADRs and adverse events can affect both physiological and pathological pathways making them difficult to distinguish. The step-wise approach below is recommended for assessing ADRs;

a) Ensure the correct medication and dosing is prescribed to the patient

b) Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient;

c) Determine the time interval between the beginning of drug treatment and the onset of the event;

d) Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.

e) Analyse the alternative causes (other than the drug) that could on their own have caused the reaction;

f) Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the National PV Centre (PPB).

Laboratory Monitoring to support Identification of ADRs Early

Regular laboratory tests for patient taking DR TB treatment is recommend in detecting and averting ADRS before clinical presentation. Detecting abnormalities in select clinical surrogate markers in a timely manner is an important step in identifying potential drug safety issues with the patient.

Risk Factors for ADRs

When evaluating and determining the ADR it is important to consider some Risk factors that could be associated with the patient.

- Advanced age
- Malnutrition
- Pregnancy and lactation
- Alcoholism
- Liver failure
- Chronic renal failure
- HIV infection
- Disseminated and advanced TB
- Allergy/Atopy
- Anaemia

- Diabetes mellitus
- Family history adverse drug reactions
- Patient receiving intermittent treatment

Patients receiving medication for other disorders, in addition to anti-tuberculosis drugs

Management of Adverse Drug reactions

Management of ADRs include reassuring the patient, drug removal or replacement, dose adjustment, symptomatic management and in some cases discontinuation of treatment depending on clinical presentation and the severity of the ADR. Proper management of ADRs is important as it may affect DR patient's adherence to their medicines, which in turn affects resistance. Hence, designing DRTB regimens should consider adverse reactions and the possibility of defaulting.

Principles in the Management of Adverse Drug Reactions

- Early identification and treat immediately & adequately
- Rule out other causes
- Consider additive or potentiating SE with concomitant therapy
- Consider drug-drug interaction
- For minor and moderate reactions: Symptomatic management (recommended algorithms, OTCs and ancillary medications)
- For moderately severe reactions: Reduce dosage/ frequency of the suspected drug.
- Severe reactions: Patient hospitalized and managed. If a reduced dose does not help to resolve stop and replace or immediate stoppage of all treatment or removal of a drug from the regime

Recording and Reporting of ADRs and Adverse events

All ADRs, adverse event and side effect need to be reported. DRTB side effects, adverse events and ADRs should be recorded in the primary source of data, which is the DRTB patient logbook. The main source of ADR data at the facility is patient logbook.

ADR reporting tools include aDSM/ADR reporting tool and PPB ADR reporting form (yellow form) (annexed Table 8.2).

Grading for ADRs

When reporting ADRS should be graded as below

Classification	Definition
Mild	The adverse drug reaction does not interfere in a significant manner with the patient's normal functioning.
Moderate	The adverse drug reaction produces some impairment in the patient's functioning but is not hazardous to the health of the patient.
Severe:	The adverse drug reaction produces significant impairment or incapacitation of functioning.
Life-threatening:	The adverse drug reaction causes extreme impairment of functioning, requiring hospitalization and if left untreated could result in the death of the patient.

Adverse drug reaction related to DR TB drugs

a) Peripheral Neuropathy

Causes of neuropathy: Cs, Lzd, H,

Grading peripheral neuropathy

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life-threatening
Neurosensory alteration (including paraesthesia and painful neuropathy)	*Asymptomatic with sensory alteration on exam or minimal paraesthesia causing no or minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing inability to perform usual social and functional activities*	*Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions*
Action	Monitor. If symptoms improve after 2 weeks, consider restarting these drugs. **Consider restarting Lzd at a lower dose.**	Stop Cs and Lzd (high dose H). If symptoms resolve after 2 weeks, consider restarting cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting cycloserine. **Do not reintroduce Lzd.**

Symptomatic relief for peripheral neuropathy:

- **Non-steroidal anti-inflammatory drugs** or acetaminophen helps alleviate symptoms.
- **Tricyclic antidepressants** have also been used successfully. Start amitriptyline 25 mg at bedtime. The dose should be increased to a maximum of 150 mg daily for refractory symptoms.
- **Carbamazepine** is effective in relieving pain and other symptoms of peripheral neuropathy.

b) Myelosuppression

Possible anti-TB drug causes: Lzd, Cfz,

Grading Myelosuppression

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Absolute neutrophil count	*1000 – 1300/ mm^3*	*750 – 999/ mm^3*	*500 – 749/mm^3*	*< 500/ mm^3*
Haemoglobin*[1]	*10.5 - 9.5 g/dL*	*9.4 - 8.0 g/dL*	*7.9 - 6.5 g/dL*	*< 6.5 g/dl*
Platelets decreased	*100.000-124.999/mm^3*	*50.000-99.999/ mm^3*	*25.000-49.000/ mm^3*	*<25.000/mm^3*
WBC decreased	*2.000-2.500/ mm^3*	*1.500-1.999/mm^3*	*1.000-1.499/mm^3*	*<1.000/mm^3*
Action	Monitor carefully, and **consider reduction of dose of Lzd (300mg daily or 600 mg thrice weekly)**	Monitor carefully, and **consider reduction of dose of Lzd to 300mg daily**; In case of Grade 2 neutropenia, **stop Lzd immediately. Restart at reduced dose once toxicity has decreased to Grade 1.**	Stop Lzd immediately. **Restart at reduced dose once toxicity has decreased to Grade 1.**	Stop Lzd immediately. **Consider haemotransfusion or erythropoietin. Restart at reduced dose once toxicity has decreased to Grade 1.**

[1] Hemoglobin should be interoperated with baseline hemoglobin value

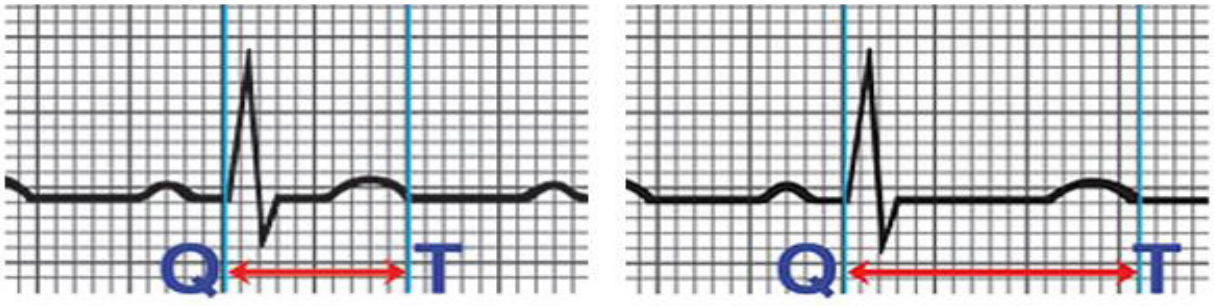
c) Prolonged QTcF Interval

Possible anti-TB drug causes: Bdq, Mfx, Lfx, Cfz

Possible other causes:

- Many other drugs can cause QT prolongation; erythromycin, clarithromycin, quinidine, ketoconazole, fluconazole, antipsychotics haloperidol, chlorpromazine, risperidone, methadone and anti-nausea drugs that include ondansetron/ granisetron, domperidone,
- Genetic causes such as long QT syndrome; hypothyroidism.

Figure 8.16: Normal vs Prolonged Q-T intervals[2]



Normal Q-T Interval *Long Q-T Interval*

Note: *The QT interval is measured from the beginning of Q-wave to the end of the T wave. Its duration varies depending on the heart rate. Its measurement must be corrected according to the heart rate. It is recommended to use the Fredericia method to calculate the QTcF (Pharmacy.umaryland.edu)*

QTcF Prolongation (ms) Gender cut-offs[3]

QTc Prolongation (ms)	Normal	Borderline	Abnormal
Men	≤ 430	431- 450	>450
Women	≤ 450	451-470	>470

[2] *https://my.clevelandclinic.org/health/diseases/17183-long-q-t-syndrome-lqts*

[3] Cite this: QTc Prolongation and Risk of Sudden Cardiac Death: Is the Debate Over? - Medscape - Feb 03, 2006.

Grading of prolonged QT interval

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life-threatening
Prolongation of QTcF	*Asymptomatic, QTcF 450 – 480 ms* *OR Increase interval **< 0.03** sec above baseline*	*Asymptomatic, QTcF 481 – 500 ms* *OR Increase in interval 0.03–0.05 sec above baseline*	*Asymptomatic, QTcF >= 501 ms without signs/ symptoms of serious arrhythmia* *OR Increase in interval ≥ 0.06 sec above baseline*	*QTcF >= 501ms or > 60 ms change from baseline and one of the following: Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia*
Action	Monitor more closely; **at least weekly ECG until QTcF has returned to grade 1 or less.**	Monitor more closely; **at least weekly ECG until QTcF has returned to grade 1 or less.**	**Stop the suspected causative drug.** Hospitalize and replete electrolytes as necessary.	**Stop the suspected causative drug**. Hospitalize and replete electrolytes as necessary.

Suggested Management strategy

Checking and replenishing serum electrolytes

- Serum potassium (K^+), ionized calcium (ionized Ca^{++}), and magnesium (Mg^{++}), should be obtained in the event a prolonged QT interval is detected.
- The cause of abnormal electrolytes should be corrected
- Whenever a low potassium is detected it should trigger urgent management with replacement and frequent repeat potassium testing (often daily or multiple times a day) to correct the levels of potassium.
- If potassium is found low, always check magnesium and ionized calcium and compensate as needed. (If unable to check, consider oral empiric replacement doses of magnesium and calcium).

d) Optic Neuritis

Possible anti-TB drug causes: Lzd, E

Grading of optic neuritis

	Grade 1 Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4 life-threatening
Visual changes (from baseline)	*Visual changes causing minimal or no interference with usual social and functional activities*	*Visual changes causing greater than minimal interference with usual social and functional activities*	*Visual changes causing inability to perform usual social and functional activities*	*Disabling visual loss*
Action	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**

Suggested management strategy

- Do not restart the suspected causative drug (Linezolid or Ethambutol)
- Refer patients to an ophthalmologist for further evaluation and management.
- Optic neuritis generally improves following cessation of offending drug, if it can be stopped early enough.

e) Hepatitis

Possible anti-TB drug causes: H, R, Z, Bdq,

Grading of Hepatitis

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
ALT (SGPT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
AST (SGOT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
ACTION	**Continue treatment regimen**. Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Continue treatment regimen.** Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Stop all drugs,** including anti-TB drugs; **measure LFTs weekly**. **Treatment may be reintroduced after toxicity is resolved.**	**Stop all drugs**, including anti-TB drugs; **measure LFTs weekly. Treatment may be reintroduced after toxicity is resolved.**

Suggested management strategy

Reintroduce anti-TB drugs once liver enzymes return to normal level. Anti-TB drugs should be reintroduced in a serial fashion by adding a new medicine every three to four days. The least hepatotoxic drugs while monitoring liver function tests after each new exposure.

Consider suspending the most likely offending drug permanently if it is not essential to the regimen. This is often the case for pyrazinamide if it is less likely to be effective by clinical history.

f) Hearing Impairment

Possible anti TB drugs causing hearing impairment: Km, Am, Cm.

Grading Hearing impairment[4]

	Grade 0: None	**Grade1: Slight**	**Grade 2: Moderate**	**Grade 3: Severe**	**Grade 4: Profound**
Decibel (dB) range	*25 dB or less*	*26-40 dB*	*Child- 31-60 *dB* *Adult- 41-60* dB*	*61-80 dB*	*>80 dB*
Severity	No/ Slight problems **Hears Whispers**	Hears/ repeats words in **normal voice** at 1 meter	Hears/ repeats words in **raised voice** at 1 meter	Hears words **shouted** into better ear	**cannot hear**/ understand shouted voice

**The grades/severity of hearing loss is also categorised differently for different age groups (see annex).*

Suggested management strategy:

Perform a monthly assessment of hearing loss and balance. Audiometry is helpful in detecting early high-frequency hearing loss that the patient may not even be aware of. If the patient is experiencing hearing loss, stop the injectable and replace it with a non-ototoxic drug. Even when non-ototoxic drugs are not available, stopping the injectable can be considered based on the patient's desire to maintain hearing. If moderate or severe vertigo, tinnitus (ringing in the ears) or vestibular disturbances arise, with or without significant hearing loss, consider decreasing frequency or stopping the injectable agent.

[4] *https://www.mtaa.org.au/hearing-background*

g) Acute Kidney Injury/Failure

Possible anti-TB drug causes

Aminoglycosides (Km, Am, Cm)

Grading Acute kidney injury/Failure

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Acute Kidney Injury/ Chronic Kidney Disease	GFR= 60-89 mL/min	GFR= 45-49 mL/min	GFR= 30-44 mL/min	GFR= 15-29 mL/min and <15 mL/min
Action	Consider **stopping injectable** until creatinine has returned to baseline. Consider **restarting the injectable at lower frequency** (e.g. MWF).	**Stop injectable** until creatinine has returned to baseline. Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**	**Stop injectable until creatinine has returned to baseline.** Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**	**Stop injectable until creatinine has returned to baseline.** Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**

** The best measure of kidney function is Glomerular Filtration Rate (GFR).*

Suggested management strategy:

Monitor serum creatinine and electrolytes frequently in patients receiving injectable. Patients with pre-existing kidney disease, diabetes, or HIV are at high risk of injectable nephrotoxicity and may be monitored more frequently.

Repeat electrolytes if necessary:

Injectable nephrotoxicity may be associated with injectable-induced electrolyte wasting. For example, it is possible to see elevated creatinine and severe hypokalaemia/ hypomagnesemia at the same time. The aetiology of this phenomenon is unclear, but it may occur more often in HIV co-infected patients. Discontinue the suspected drug (usually the injectable). If the acute renal failure is severe, then stop all drugs. Follow serum creatinine and electrolytes closely until the creatinine has returned to baseline or has stabilized. Consider strict weight-based dosing of the injectable if the patient's weight is less than 50 kg. Suspend the injectable permanently if the nephrotoxicity recurs despite intermittent dosing, and add additional anti-TB drugs to reinforce the regimen.

h) Hypokalaemia

Possible anti-TB drug causes: Cm, Km, Am

Normal values of potassium level and quantity of KCL required

Potassium level Normal value (3.5-5.0 Meq/L)	Quantity of KCl
3.7 or more	None
3.4-3.6	40 meq
3.0-3.3	60 meq
2.7-2.9	80 meq
2.4-2.6	80 -120 meq
2.0-2.3	60 meq IV and 80 meq PO
<2.0	60 meq IV and 100 meq PO

Grading Hypokalaemia

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Hypokalaemia	3.4 - 3.0mmol/L	2.9 – 2.5 mmol/L	2.4 - 2.0 mmol/L or intensive replacement therapy or hospitalization required	< 2.0 mmol/L or abnormal potassium with paresis, ileus or life-threatening arrhythmia
Action	**Continue injectable.** **Start oral potassium replacement therapy**. **Check serum magnesium and replace if necessary**	**Continue injectable**. **Start aggressive oral potassium replacement therapy.** **Replace magnesium as necessary**.	**Consider stopping the injectable temporarily**. **Start IV potassium replacement therapy in addition to oral**. **Replace magnesium and other electrolytes as necessary**.	**Stop injectable** temporarily. **Start IV potassium replacement therapy** in addition to oral. **Replace magnesium** and other electrolytes as necessary.

8.11. WHO Grouping of DRTB medicines with common adverse drug reactions

Group A - WHO 2018 grouping of medicines for longer MDR-TB Regimens			
Drug	**Activity against TB, Mechanism of action, and metabolism**	**Common Adverse Drug Reactions**	**Contraindications and special consideration**
Group A - WHO 2018 grouping of medicines for longer MDR-TB Regimens			
Levofloxacin (Lfx)	**Bactericidal:** has strong anti-TB activity. Cross-resistance with other fluoroquinolones but may not be complete. Data suggests greater activity than ciprofloxacin or Ofloxacin. Inhibits DNA gyrase	Nausea and bloating. Headache, dizziness, insomnia or tremulousness. Rare tendon rupture, arthralgia (can usually be treated symptomatically). Moderate QTcF prolongation, hypoglycaemia	Fluoroquinolones intolerance, prolonged QTcF, pregnancy (relative contraindication).
Moxifloxacin (Mfx)	**Bactericidal:** inhibits DNA gyrase; cross-resistance with other fluoroquinolones, but may be more active based on in vitro data	Nausea and diarrhoea. Headache and dizziness. Rare tendon rupture; arthralgia. Rare hepatotoxicity. QTc Prolongation, hypo/ hyperglycaemia	Fluoroquinolones intolerance, prolonged QTc
Bedaquiline (Bdq)	**Bactericidal:** Inhibits ATP synthesis. Mainly eliminated in faeces.	Nausea, vomiting, abdominal pain, loss of appetite, joint pain, headache. QT prolongation, hyperuricemia, phospholipidosis, elevated aminotransferases.	Do not use or discontinue Bedaquiline: Clinically significant ventricular arrhythmia. A QTcF interval of >500 ms Severe liver disease. Abnormal electrolytes. Use with caution in the following situations: Use with other QT prolonging drugs (see drug interactions) A history of torsade de pointes A history of congenital long QT syndrome A history of hypothyroidism and Brady arrhythmias A history of uncompensated heart failure Serum calcium, magnesium or potassium levels below the lower limits of normal

Linezolid (Lzd)	Has in vitro **bactericidal activity** – increasing clinical experience7; inhibits protein synthesis	Myelosuppression Diarrhoea and nausea. Optic and peripheral neuropathy Lactic acidosis – patients who develop recurrent nausea or vomiting.	Hypersensitivity to Oxazolidinones Symptoms of neuropathy (pain, numbness, tingling or weakness in the extremities
Group B - WHO 2018 grouping of medicines for longer MDR-TB Regimens			
Clofazimine (Cfz)	In vitro activity against *M. tuberculosis* without much in vivo data. Generally reserved for cases with few other options. Tissue half-life estimated to be around 70 days	Discoloration of skin, conjunctiva, cornea and body fluids. Dry skin, pruritus, rash, ichthyosis, and xerosis. Gastrointestinal intolerance. Photosensitivity.	Allergy to Clofazimine Electrolytes should be monitored and replaced if vomiting is severe In the case of Gastritis, dosing on antacids should be carefully times (> 2 hours apart) so as not to interfere with the absorption of anti-TB drugs
Cycloserine (Cs)	**Bacteriostatic:** inhibits cell wall synthesis	**CNS toxicity:** including seizure, depression, psychosis and suicidal ideation Other side effects include peripheral neuropathy and skin changes.	Relative contraindications include seizure disorder, psychotic disease or alcohol abuse Initiate anticonvulsant therapy (e.g. valproic acid, phenytoin, phenobarbitone) to address the side effects associated with CNS toxicity Increase pyridoxine to 300mg daily Lower the dose of the suspected agent or discontinue or replace the suspected agent if this can be done without compromising the regimen For psychotic symptoms, initiate antipsychotic drugs and halt administration of Cs for 1-4 weeks while symptoms of psychosis are brought under control. Lower the dose if this can be done without compromising the regimen
Group C - WHO 2018 grouping of medicines for longer MDR-TB Regimens			
Imipenem-cilastatin	Given that imipenem is rapidly degraded by renal proximal tubule dipeptidases, it is used in combination with the dipeptidases inhibitor, cilastatin. (Conversely, meropenem a similar drug as imipenem is stable to renal dipeptidases and requires no cilastatin). Cilastatin is partially metabolized renally.	**Common:** Diarrhoea, nausea, or vomiting. **Less common:** Seizure (noted with CNS infection), palpitations, pseudomembranous colitis.	Carbapenems intolerance; meningitis (use meropenem rather than imipenem).

Meropenem	In vitro activity – very limited clinical experience (meropenem is stable to renal dipeptidases and requires no cilastatin).	Diarrhoea, nausea or vomiting. Seizure (noted with CNS infection), but rare compared to imipenem. Rarely elevated LFTs, hematologic toxicity, hypersensitivity	Carbapenems intolerance
***Delamanid (Dlm)**	Inhibition of the synthesis of the mycobacterial cell wall components, methoxy-mycolic and keto-mycolic acid. Delamanid disappears from plasma with a t1/2 of 30-38 hours. Delamanid is not excreted in urine.	Nausea, vomiting, and dizziness. QT prolongation	**Do not use or discontinue Delamanid** • Clinically significant ventricular arrhythmia. • A QTcF interval of > 500 ms (confirmed by repeat ECG). • Severe liver disease. • Serum Albumin less than 2.8. • Abnormal electrolytes. **Use with caution in the following situations (with more frequent ECG monitoring and evaluation of risk versus benefit):** • Use with other QT prolonging drugs (see drug interactions). • A history of torsade de pointes. • A history of congenital long QT syndrome. • A history of hypothyroidism and Brady arrhythmias. • A history of uncompensated heart failure. • Serum calcium, magnesium, or potassium levels below the lower limits of normal. **Use with caution in patients sensitive to lactose**
Ethambutol (Emb)	**Bacteriostatic:** inhibitor of cell wall synthesis; bactericidal only at the high end of the dosing range. At doses used over long periods of time, Ethambutol protects against further development of resistance	Retro bulbar neuritis (dose-related – exacerbated during renal failure).	Pre-existing optic neuritis; Visual changes on Ethambutol

Pyrazinamide (Pza)	**Bactericidal** for semi-dormant M. tuberculosis. Mechanism unclear	Gout (hyperuricemia) and arthralgia. Hepatotoxicity. Rash. Photosensitivity. Gastrointestinal upset	Allergy to pyrazinamide; severe gout
Amikacin (Am)	**Bactericidal:** Inhibits protein synthesis. Excreted primarily unchanged through the kidney.	Nephrotoxicity, Ototoxicity	Relative contraindication in pregnancy and Hypersensitivity to aminoglycosides Caution with renal, hepatic, vestibular or auditory impairment.
Prothionamide (Pto)	**Weakly bactericidal:** blocks mycolic acid synthesis	Gastrointestinal upset and anorexia: Metallic taste. Hepatotoxicity. Endocrine effects: Gynaecomastia, hair loss, acne, impotence, menstrual irregularity, and reversible hypothyroidism	Side effects may be exaggerated in patients also taking Cycloserine For hypothyroidism, initiate L-thyroxine therapy (50-100 mcg/ day). If there is no possibility of switching, monitor TSH for thyroxine.
Kanamycin (Km)	**Bactericidal:** has strong anti-TB activity. Cross-resistance with Amikacin and some data suggesting cross-resistance with Capreomycin; inhibits protein synthesis	Nephrotoxicity: Ototoxicity (hearing loss) and vestibular toxicity: Increases with advanced age and prolonged use	Pregnancy (congenital deafness seen with streptomycin and Kanamycin use in pregnancy); hypersensitivity to aminoglycosides; caution with renal, vestibular or auditory impairment; patients with intestinal obstructions.
Para-amino salicylic acid (PAS)	**Bacteriostatic.**	Gastrointestinal distress Rare hepatotoxicity and coagulopathy Reversible hypothyroidism	Pregnancy (relative).
Others			
Isoniazid (Inh)	**Bactericidal:** Especially for rapidly dividing cells. Affects mycolic acid (cell wall) synthesis. Inclusion of isoniazid in the regimen of patients with strain W MDR-TB was also associated with improved outcomes	**Hepatitis** (age-related). Peripheral neuropathy. Hypersensitivity reactions. Other reactions, including optic neuritis, arthralgia, CNS changes, drug-induced lupus, diarrhoea, and cramping with liquid product	**Patients with high-level isoniazid resistance** who have failed an isoniazid-containing regimen should not receive isoniazid. History of allergic reaction to isoniazid

Rifampicin (Rif)	**Bactericidal:** inhibits protein synthesis; cross-resistance with other Rifamycins	Orange staining of body fluids Rash and pruritus Gastrointestinal upsets, flu-like syndrome Hepatotoxicity. Haematological abnormalities (thrombocytopenia, haemolytic anaemia).	**Rifamycins allergy;** due to drug interactions, may be contraindicated with concurrent use of certain drugs
Rifapentine (Rpt)	**Bactericidal:** same mechanism of action as Rifampin, inhibits RNA polymerase. 100% cross-resistant with Rifampin.	Red–orange staining of body fluids Rash and pruritus Hypersensitivity reaction Hepatotoxicity Haematological abnormalities	History of hypersensitivity to any of the Rifamycins (i.e. Rifampin or Rifabutin)

8.12. Post treatment Follow up

Month (after treatment completion)	3	6	12	18	24
Screening for substance abuse	X	X	X	X	X
Review by a Clinician	X	X	X	X	X
Weight/ BMI	Done at each follow up visit				
GeneXpert (for presumptive DRTB)	X	X	X	X	X
Culture (For presumptive DR TB)	X	X	X	X	X
1st line DST	Done for any culture positive patient on follow up				
2nd line DST	Done for any culture positive patient on follow up				
CXR/ Chest CT scan	Done for any presumptive DRTB patient on follow up				
Spirometry	Done as clinically indicated (when there is impairment of lung function)				

NON-TUBERCULOUS MYCOBACTERIUM (NTM)

9

9.1. Epidemiology

These are free-living organisms found in air, water and soil from where they cause infection. Zoonotic spread can occur from domestic and wild animals. There is no person-to-person spread documented with paucity of data in most of the world since it is not a notifiable disease. The prevalence of NTM is rising, as that of *M. tuberculosis* is going down; possible causes include:

- Improvements in diagnostics: better clinical recognition of the disease.
- Development and wider use of diagnostic support tools (such as CT scan, new laboratory methods)
- Better characterization of mycobacteria, along with greater disease awareness
- The worldwide HIV epidemic and the increase in number of immunocompromised hosts
- The increase in chronic lung diseases

NTM can cause pulmonary disease (NTM-PD) in vulnerable persons and can contaminate clinical samples due to harmless colonization. Over 150 NTM species have been described while over 60 species cause human disease, the majority of which are resistant to most anti-tuberculous drugs. NTM-PD can be classified based on culture speed:

1. Rapidly growing NTM - *M. abscessus*
2. Slowly growing NTM - *M. avium complex*, *M. kansasii*, *M. xenopi*, *M. malmoense*

9.2. Associated risk factors

Risk factors for developing NTM-PD include the following:

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

9.3. Clinical presentation

Symptoms of NTM-PD (Pulmonary Disease) are very similar to PTB and are impossible to distinguish clinically, thus the basis for performing culture:

- Chronic cough - dry, productive or hemoptysis
- Fever
- Night sweats
- Weight loss and wasting

9.4. Investigations (Important considerations)

- Sputum smear exam and Mantoux test may be positive in both MTB and NTM infection.
- GeneXpert will detect MTB **BUT WILL NOT** detect NTM. (*In patients with positive AFB sputum smear and a negative GeneXpert result for MTB, consider NTM and culture*).
- Chest X-ray and other imaging 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.

9.5. Management of NTM

The decision to start treatment should be influenced by the severity of NTM-pulmonary disease, the risk of progressive NTM-pulmonary disease, the presence of comorbidity and the goals of treatment. Decision to treat remains **individualized** with DNTLD/P consultation and individuals may require a period of longitudinal assessment (symptoms, radiological change and mycobacterial culture results) to inform NTM treatment decisions.

To determine the clinical relevance of NTM positive cultures, it is essential to distinguish transient or persistent colonization (which is usually not treated) from true infection or disease. Use of the ATS / IDSA 2007 definition of NTM-pulmonary disease is recommended to define disease as shown in the table below.

Table 9.1: Definition of NTM-Pulmonary disease

Clinical and microbiological criteria for diagnosing non-tuberculous mycobacterial lung disease	
Clinical (both required)	1. Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or an HRCT scan that shows multifocal bronchiectasis with multiple small nodules. and 2. Appropriate exclusion of other diagnoses
Microbiological	1. Positive culture results from at least two separate expectorated sputum samples. (If the results from the initial sputum samples are nondiagnostic, consider repeat sputum AFB smears and cultures.) or 2. Positive culture results from at least one bronchial wash or lavage. or 3. Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture positive for NTM. 4. Expert consultation should be obtained when NTM are recovered that are either infrequently encountered or that usually represent environmental contamination. 5. Patients suspected of having NTM lung disease but who do not meet the diagnostic criteria should be followed until the diagnosis is firmly established or excluded. 6. Making the diagnosis of NTM lung disease does not, *per se*, necessitate the institution of therapy, which is a decision based on potential risks and benefits of therapy for individual patients.

Management of NTM-PD depends on the type of NTM cultured as shown in Table 9.2.

Table 9.2: Management of NTM-PD

Mycobacteria species	Drugs used for treatment	Treatment duration
***Mycobacterium avium* complex**	• Nodular/bronchiectatic disease: Clarithromycin 1gm/Azithromycin 500mg, Rifampin 600 mg and Ethambutol 15-25mg/kg, thrice weekly or daily (severe disease), +/-Amikacin in the first 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 • For Clarithromycin resistant disease: Rifampin 600mg, Ethambutol 15-25mg/kg,Isoniazid 300mg/Moxifloxacin 400mg daily +/-Amikacin in the first 3 months	Treat until culture negative on therapy for 1 year. Treat until CD4 above 100 in HIV co-infection
M. fortuitum	• Any 2 of the following drugs: Amikacin, fluoroquinolones, sulfonamides, imipenem, 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 of 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	Treat until sputum cultures negative for more than 6 months
M. szulgai	• Responds to treatment • Combinations of rifampicin, ethambutol and clarithromycin	Treaty until cultures are negative
M. malmoense	• Not very responsive to treatment • Clarithromycin, rifampicin and ethambutol had better response and less mortality	At least 2 years

TUBERCULOSIS INFECTION PREVENTION AND CONTROL (IPC)

10

10.1 Introduction

Infection prevention and control is a critical component of End TB strategy and primarily focuses on decreasing the risk of TB transmission. TB Infection prevention and control (TB IPC) in the health care settings is therefore an important step forward in the efforts to prevent transmission of TB. Good TB IPC practices which include administrative, environmental and respiratory controls can make health care safer, by protecting patients, clients, HCWs and community from Tuberculosis.

Additionally, IPC becomes more important in control against transmission of TB, drug resistant TB (DR-TB) and other infectious respiratory conditions like Covid-19

KEY HIGHLIGHTS:

Levels of TB infection control measures include:

I. **Administrative (managerial) control measures**

II. **Environmental control measures**

III. **Personal protective equipment (respiratory protection).**

- **Administrative control measures**
  - Patient's triage
  - Controlled flow of movement within the facility
  - Triaging of hospitalized patients
- **Environmental Control Measures**
  - Natural ventilation
  - Mechanical ventilation
- **Personal protective Equipment (respiratory protection)**
  - Refers to items specifically used to protect the health care provider, the patient and the community from exposure
  - They go hand in hand with administrative and environmental measures

10.2 TB Infection prevention control measures

10.2.1 Levels of TB infection control measures

The TB infection control should be based on a three-level hierarchy of control measures and include:

I. Administrative (managerial) control measures

II. Environmental control measures

III. 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 control measures. Each level operates at a different point in the TB infection control process.

The levels of operation include;

First priority; Administrative control measures reduce health care workers and patient exposure to infectious droplet nuclei

Second priority; Environmental control measures reduce the concentration of infectious droplet nuclei

Third priority; Personal protective equipment (respiratory protection) protects HCWs, patients and family members in areas where the concentration of droplet nuclei cannot be adequately reduced by administrative and environmental control measures.

10.2.2 Administrative (Managerial and Policy) Control Measures

Administrative measures are defined as the managerial or work practices (e.g., early diagnosis, prompt isolation or separation of potential TB patients, prompt initiation of anti-tuberculosis treatment and minimize aerosol-generating procedures) to significantly reduce the risk of TB transmission by preventing the generation of droplet nuclei or reducing exposure to droplet nuclei. They include:

A.Patients triage

Upon entry into the health facility, a member of the medical staff should identify patients with a cough as soon as possible. All patients with cough should receive tissues or face masks, and they should be advised on cough etiquette.

B.Controlled flow of movement within the facility

Inside the TB department, circulation of patients and attendants should be controlled

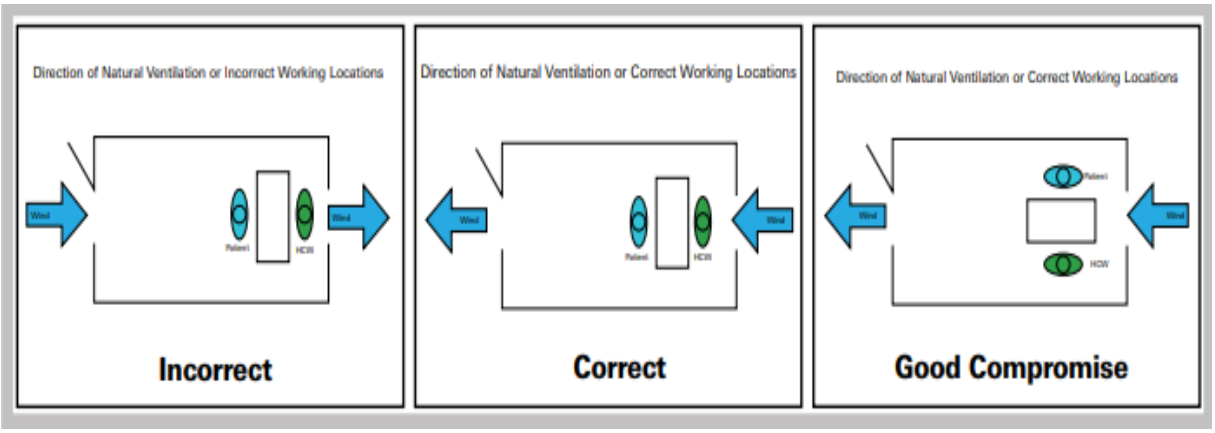


Figure 10.1: Direction of natural ventilation/ correct working setup

Encourage patients/attendants to spend as much time as possible outdoors if weather permits or in areas that are open.

In addition,

- Have visible signage on entry doors to TB wards that caution visitors as they enter.
- Limit visitation duration, particularly for contagious patients.
- Encourage visits outside the building, especially for contagious patients.
- Have visiting areas well identified with signage.
- Before any visit, the nurse should provide information on transmission risk, including the usage of respirators if caregivers need to go in high risk areas, such as smear-positive, drug- resistant TB (DR-TB), re-treatment smear-positive inpatient units and areas or clinics where diagnosis of TB is being undertaken.
- Restrict entry for persons most at risk of infection including young children, the elderly and the immunocompromised.
- Avoid contact with known index cases or restrict movement of potentially infectious TB patients to areas where they may infect other patients, and vice versa. Equally patients without TB should not be permitted in areas where they are unnecessarily exposed to TB.

C.Triaging of hospitalized patients

TB care is primarily an ambulatory care and patients should preferably be treated as outpatients. Hospitalization should be limited to critically unwell patients. Wards attending to TB patients must be separated from the other wards in the health facility. Ideally, within the TB department, patients should be placed in single rooms. If this is not possible, cohort isolation must be implemented and different sections should be labelled according to the degree of contagiousness (smear/culture status) and risk of resistance.

NOTE:

All TB inpatient facilities should have an isolation room. If none exists, a very high priority is to establish one. *(Refer to the TB isolation policy).*

Bacteriologically confirmed TB patients and suspected DR-TB patients, including chronic cases and re- treatment cases that are likely to have DR-TB should have single isolation rooms. It is particularly important not to mix DR TB patients with other patients. Where possible, presumptive TB cases should not be hospitalized for diagnosis. If hospitalization is necessary, these patients need isolation rooms.

Components to good work practice (and administrative) controls

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. This is done using TB Infection control assessment tool ***Annex 6.1: TB Infection control assessment tool***

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.

Composition of IPC Committee (County, Sub county and Facility Level)

IPC team should include expertise in:

- Administration
- Infection Prevention Control
- Clinical
- Epidemiology
- Laboratory
- Medical engineering
- Occupational health

IPC team should be responsible for all aspects of the facility TB IPC plan development, implementation and review

c) Steps for patient management to prevent transmission of TB in community, workplace and health care settings

Table 10.1: Steps for patient management

Step	Action	Description
1.	**Screen**	Early identification of presumptive TB patients or confirmed TB patients. This can be achieved by assigning a health worker to screen patients for TB immediately when they arrive at the facility.
2.	**Educate**	Instruct all patients with chronic cough on cough hygiene i.e. covering the mouth and nose when coughing or sneezing, where possible use face masks or tissues to assist them in covering their mouths. Educate on safe sputum disposal methods
3.	**Separate**	Presumptive TB clients and TB 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 presumptive patients or samples can be referred.
5.	**Treatment**	Confirm the diagnosis of TB disease within 2 hours for sputum smear microscopy and Gene Xpert results and 2-6 weeks for culture. Patients diagnosed with TB should be started on anti-TB treatment as soon as possible

6.	**Discharge Plan**	For inpatient and outpatient settings, coordinate a discharge plan with the patient for continuity of care

10.2.3. 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. Opening windows and doors is the most practiced form of environmental control.

There are two types of environmental controls: -

A. 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.*

B. 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 triaging 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
    - Health care staff should be mindful of the direction of airflow to ensure the patient is closest to the exhaust fans and the staff are closest to the clean air source. This arrangement should be done every morning.
    - Promotes air-flow patterns from the least infected (health care worker) to the most infected (patients)
    - Maximize natural draught through chimney affects ventilation grills, open verandas

3. **Maximize availability of sunlight as a natural deterrent to growth of MTB colonies**

C. Dilution

This is the simplest, extremely effective, and least expensive technique. It involves removal and dilution of infectious air by maximizing natural ventilation

D. Filtration

It's a method that involves removing infectious particles and brings back filtered air. This involves the use of HEPA cleaner (High Efficiency Particulate Air cleaner).

- In-duct application
- In conjunction with Room air cleaner (mobile or fixed)

E. Purification

It involves the use of Ultraviolet Germicidal Irradiation (UVGI) to inactivate M. tuberculosis organisms

F. Disinfection

This involves the process of eliminating many or all pathogenic microorganisms, except bacterial spores, on inanimate objects.

It includes,

- Chemical disinfection for general equipment and surfaces
- Thermal disinfection e.g. steam sterilization or autoclaving

If there are inadequate or insufficient administrative control measures, environmental control measures will **not** eliminate the risk.

10.2.4. Personal protective Equipment (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 in the line of duty providing or seeking services.

They include; gloves, aprons, gowns, caps, surgical masks, respirators and protective eyewear.

Respiratory protection is an important aspect for protecting HCWs against TB nosocomial infection. It goes hand in hand with administrative and environmental measures.

This measure is important in high risk areas such as DR-TB treatment facilities, centers handling presumptive TB and DR specimens, surgical centers handling bronchoscopy and autopsy, sputum induction and other aerosol –generating procedures plus people handling disposal waste from the laboratory and wards.

Table 10.2: 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 performing sputum induction 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 attending to patients with infectious disease • When handling contaminated waste	Service providers, patients
N-95 masks	• When handling patients with airborne or droplet infections	Service providers, visitors and caregivers
Surgical/ Procedural masks	• When performing invasive procedures • When handling medical waste	Patients, service providers
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	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 the mouth using tissues or clothes, not spitting on the 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.

- The N95 masks can be re-used repeatedly if they are properly stored.
- 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.

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.

10.3. Tuberculosis Laboratory Safety

KEY HIGHLIGHTS:

- **Sputum microscopy is a low-risk activity; Biosafety Cabinets are not mandatory for performing direct sputum-smear microscopy.**
- **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.**
- **Respirators and surgical masks are not the same. Surgical masks provide no effective respiratory protection from aerosols and must not be used.**

Laboratory facilities are designated as:

- **Basic** – Biosafety Level 1(Smear microscopy for AFB, Gene Xpert)
- **Basic** –Biosafety Level 2 (Smear microscopy for AFB, Gene Xpert, LPA)
- **Containment** – Biosafety Level 3 (Smear microscopy for AFB, Gene Xpert, LPA, culture and phenotypic DST)
- **Maximum containment** – Biosafety Level 4(Marburg virus, Corona Virus, Ebola virus etc).

Biosafety level designations are based on a composite of the design features, construction, containment facilities, equipment, practices and operational procedures required for working with agents from the various risk groups.

10.3.1 Risk level and laboratory areas

The entry area should be reserved for 'clean' activities. 'Dirty' activities should be furthest away from the entry.

Low-risk activities include:

- Administration, hand-washing station, microscopy, Gene Xpert, consumables and reagent storage, staining.

Moderate-risk activities include:

- Culture processing and media inoculation.

High-risk activities include:

- Handling positive cultures, identification of MTB, DST, preparing DNA Extracts from positive cultures.

Table 10.3: Risk levels and assessments of risk in TB laboratories

RISK LEVEL	LABORATORY ACTIVITIES	ASSESSMENT OF RISK	SAFETY EQUIPMENT
Low risk	Direct sputum microscopy; preparation of specimens for the Xpert MTB/RIF assay	Low risk of generating infectious aerosols from specimens; low concentration of infectious particles	Handwashing/Eye wash station
Moderate risk	Processing and concentration of specimens for inoculation on primary culture media; direct molecular testing on processed sputum by a line probe assay	Moderate risk of generating infectious aerosols from specimens; low concentration of infectious particles	Handwashing/Eye wash station Biosafety cabinet(BSC) Autoclave
High risk	Culture manipulation for identification, phenotypic DST, or a line probe assay on cultures	High risk of generating infectious aerosols from cultures; high concentration of infectious particles	Handwashing/Eye wash station Biosafety cabinet(BSC) Autoclave Biosafety level 3 lab

Risk assessment for TB laboratories

Decisions about which are the most appropriate biosafety measures for a specific laboratory should be undertaken using an approach based on risk assessment that considers the different types of procedures performed by the laboratory.

The risk-assessment approach for a TB laboratory considers:

- The workload (No. slides examined microscopically per day)
- The bacterial load of materials (such as sputum specimens and cultures), and the viability of TB bacilli

- Possible route of transmission for TB
- Whether the material handled and the manipulations required for each procedure are likely to generate infectious aerosols
- The number of maneuvers for each technique that may potentially generate aerosols
- The workload of the laboratory and individual staff members
- The location of the laboratory
- The epidemiology of the disease and the patient population served by the laboratory
- The level of experience and the competence of the laboratory's technicians
- The health of the laboratory's workers (especially HIV-positive technicians)

10.3.2 Personal protective equipment in the laboratory

Masks: One of the greatest false beliefs is that a standard surgical mask will protect the wearer from becoming infected with TB. These masks are made from porous material that will not trap TB bacilli, and have an extremely poor fit creating large gaps between the face and mask.

Surgical masks provide no respiratory protection from aerosols and must not be used in a laboratory setting.

Respirators: Respirators must filter >95% of infectious particles greater than 0.2µm in size. N95 and FFP2 respirators meet the requirements and are lightweight, disposable devices that cover the nose and mouth.

Both FFP2 and N95 respirators may be 'valved' or 'unvalved'

- 'Valved' respirators allow expired air to move easily from the lungs to the environment but closes when breathing in occurs
- 'Unvalved' respirators do not have a valve.

Respirators are not usually required for work in a TB culture laboratory. However, they must be worn when setting up DST.

They can be reused provided that they are properly worn, stored and cared for.

RESPIRATORS ARE NOT A SUBSTITUTE FOR A PROPERLY MAINTAINED AND FUNCTIONING BIOLOGICAL SAFETY CABINET

If respirators are used, staff must be

- Instructed in correct use
- Taught how to care for a respirator.

Gloves: Disposable gloves only are to be worn in a TB laboratory.

DO NOT RE-WEAR USED GLOVES

Several pairs of gloves will be used each day; a sufficient supply must be readily available.

Gloves must be worn for all procedures that involve contact with specimens or laboratory items used in handling specimens or cultures.

Allergic reactions such as skin rash (dermatitis) and hypersensitivity reactions may occur in staff wearing latex gloves (powdered and non-powdered). Alternative glove materials include vinyl and nitrile which rarely cause allergic reactions.

DO NOT TAKE GLOVES OUTSIDE OF THE LABORATORY

Wearing and removing gloves:

Different sizes of gloves must be available (small, medium, large). Poorly fitting gloves reduce the dexterity of the fingers and increase the risk of glove contamination and accidents.

- Too small and they are easy to tear
- Too large and fine motor skills are lost

Used gloves must be discarded into a laboratory infectious waste bin.

Once gloves are removed, wash your hands immediately.

Laboratory Coats and Gowns: Laboratory Coats must be worn at all times when working in the laboratory and various sizes should be provided.

They should be tied at the back, not the front, and be made from water-resistant materials to avoid liquids soaking into the gown.

LABORATORY COATS MUST NOT BE WORN OR CLEANED OUTSIDE THE LABORATORY

- Reusable gowns must be autoclaved (121˚C for 15 minutes) before being taken away for cleaning
- For re-usable gowns, there should be at least three gowns available per staff member
  - In-use
  - Being cleaned
  - Ready for use

- Gowns should be changed weekly or after an obvious spill occurs
- Gowns must be available in small, medium, and large sizes

Coats

Laboratory coats are open at the front and may have short or long sleeves.

NEVER CARRY LABORATORY COATS HOME.

10.3.3 Safety precaution in sputum smears preparation

- The major risk of TB infection in the laboratory is associated with inhalation of aerosols generated by laboratory processes. Minimizing their production is the most effective means of staying safe.
- Sputum microscopy is a low-risk activity; Biosafety Cabinets are not mandatory for performing direct sputum-smear microscopy.
- With good microbiological technique, direct sputum-smear microscopy entails a low risk of generating infectious aerosols, and such procedures may therefore be performed on an open bench, provided that adequate ventilation can be assured
- Where good laboratory practices are used, risk of infection to laboratory technicians is very low during smear preparation.
- A higher risk of infection exist when collecting sputum specimens from patients.
- Aerosols may be produced in the TB laboratory when handling leaking specimens, opening sample containers, and preparing smears. When care and appropriate techniques are used, handling sputum presents a minimal risk of acquiring infection to a technician.
- For laboratory staff, the greatest risk of infection involves sputum collection. People with presumptive TB may cough and in doing so, spread TB bacilli in tiny droplets in the air which may infect others when they are inhaled. Precautions must be taken to minimize this exposure.
- The laboratory technician is at considerably more risk when sputum is processed for culture and drug susceptibility testing. These procedures require shaking and centrifugation
- Consequently, special equipment such as biological safety cabinets, which are costly to purchase and maintain, are required. However, this equipment is not justified in the AFB smear microscopy laboratory.

Proper collection of sputum: If a coughing patient comes into the laboratory, ask them to cover their mouth.

CAUTION!

NEVER COLLECT SPUTUM SPECIMENS IN LABORATORIES, TOILETS, WAITING ROOMS, RECEPTION ROOMS, OR ANY OTHER ENCLOSED SPACE.

Wherever possible, collect specimens outside where air movement will rapidly dilute infectious droplets and UV rays from the sun will rapidly inactivate TB bacilli.

Sputum collection areas

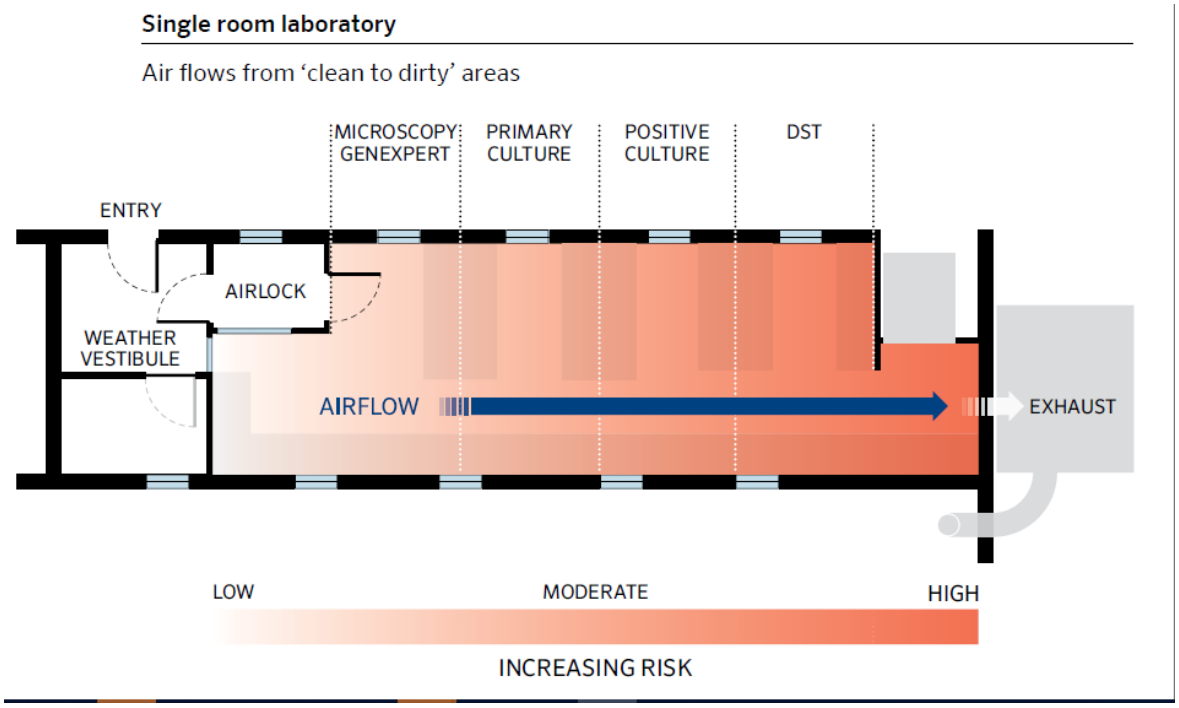
Designated sputum collection areas should be clearly marked and wherever possible, outside in open air where bacilli will naturally be dispersed by wind rather than in a closed room where the concentration of bacilli will be high.

Designated sputum collection booths can be established with instructions on steps in collecting a good sputum sample posted on the wall.

Laboratory arrangement: The TB laboratory should be a well-ventilated area which is dedicated to microbiology with restricted access. The air movement should consider the following;

- Directional airflow that helps reduce risk. It is created using a negative pressure gradient.
- Air should move from the entry, where low risk activities take place, to the end of the laboratory where the highest risk activities occur.

Establish airflow in working areas that will direct potentially infectious particles away from personnel. Air must be exhausted into a remote area. An extraction fan can be useful to vent air from a smear preparation area with poor ventilation that is closed off due to extreme climatic conditions.



Appropriate Disinfectants: Phenolic agents (5% phenol in water or a phenolic disinfectant product diluted as per label) are excellent disinfectants for cleaning up sputum spills and for decontaminating equipment and single use items prior to disposal. Fresh household bleach (5% sodium hypochlorite) diluted 1:10 with water can also be used as a general disinfectant. Bleach solution works well for cleaning up blood spills; however, it is somewhat less effective than phenolic agents against TB. It is important that bleach dilutions be made fresh since it loses potency with time. 70% alcohol is a good agent for cleaning bench tops.

Safe disposal of infectious waste

After smears have been processed, place all infected materials including closed sputum containers in a biohazard bag (polyethylene, if available). Discard applicator sticks used for smearing immediately after use. Since all sputum specimens are considered potentially infectious, treat all materials in the procedure as contaminated.

Discard specimens by one of the following methods:

- Incineration
- Burying
- Autoclaving

To protect the surrounding population, the laboratory must dispose of waste safely. Incineration is usually the most practical way for safe destruction of laboratory waste. If incineration cannot be arranged, discard the waste in a deep pit of at least 1.5-meter depth. If an autoclave is available, place infected materials inside and follow procedures for safe and adequate sterilization.

Ventilated Cabinets

Ventilated Cabinets include Laboratory Fume Hoods and Biological Safety Cabinets.

The details of these devices follow.

1. Laboratory Fume Hoods

The least expensive ventilated cabinet for laboratories is the Laboratory Fume Hood. This type of environmental control is designed for the purpose of worker protection (no protection of the environment or the product [specimen/ culture]). These devices, like Biological Safety Cabinets, are designed to minimize worker exposures by controlling emissions of airborne contaminants (including aerosols) through the following:

- The full or partial enclosure of a potential contaminant source
- The use of airflow velocities to capture and remove airborne contaminants near their point of generation.
- The use of air pressure relationships that define the direction of airflow into the cabinet

2. Biological Safety Cabinets (BSC)

BSCs are categorized as Class I, Class II, or Class III.

Class I

Class I BSCs draw unfiltered room air through the front opening, passing it over the work surface, and expelling it through an exhaust duct and through a HEPA filter.

Class I BSCs protect the worker but do not protect the work area against contamination because unfiltered room air is drawn into the cabinet and over the work surface.

Class II

Class 2 BSCs draw around 70% of purified air from the HEPA filter above the work area and around 30% air through the front grille.

Class II provides protection for the **user, environment** and **the work area.** There are four types of BSC Class II: A1, A2, B1 and B2. The most suitable for all TB work is the type A2.

Class III

Also known as glove boxes, generally they are installed only in maximum containment laboratories.

Do not use class III BSCs in TB laboratories..

One of the most persistent myths held by laboratory staff the world over is that a BSC provides complete protection from the infectious material it contains. **THIS IS NOT TRUE!!!**

GOOD SAFE WORKING PRACTICE IS YOUR BEST PROTECTION

Poor technique when using a BSC will expose you to potential infection.

- **A BSC can maintain the level of sterility you create, it cannot produce it by itself**
- **Your actions must always complement the operation of the BSC**
- **You prevent cross-contamination by using safe working practice.**

Certification of BSCs

To check its performance a BSC must be certified at least annually.

A qualified engineer must assess the BSC using an accepted national or international standard. The engineer will decontaminate the BSC before inspection.

It is the responsibility of the laboratory manager to organize certification and to advise staff that the BSC may be safely used.

It is the responsibility of the county management to support annual certification of biosafety cabinets

BSC certification is required

- Before first use of a newly-installed BSC
- Annually
- When a BSC is moved within the laboratory
- Whenever a HEPA filter is replaced
- Whenever components within the plenum are replaced

Once certification is done, it must be displayed on the BSC.

10.4. Infection prevention at radiology departments

Appropriate placement of patients with TB in an isolation room reduces the risk of infection and disease to HCWs.

The patient should be explained and instructed to wear a surgical mask at all times while being wheeled to the radiology department.

10.5. Prevention and control of TB transmission within the community

Increase awareness on reducing transmission of TB in the community by creating community awareness, early identification of Presumptive TB and referral for follow-up in the health care setting.

Identified TB cases should be taught on cough etiquette and cough hygiene. Create Community awareness on the importance of adherence to TB treatment.

10.6. IPC in congregate settings

There are special settings in the community that are of high risk and call for special attention as far as TB infection, prevention and control is concerned. TB is spread more readily in congregate settings and this is because of longer duration of potential exposure, crowded environment, poor ventilation, and limited access to health care services.

These include:

- Prisons and remand cells
- Informal settlements (slums)
- Refugee and internally displaced persons (IDP) camps
- learning institutions (schools, colleges)
- Security forces training camps (military, General Service Unit (GSU), Police, National Youth Service (NYS) etc

Correctional facilities (Prisons and Remands)

All inmates on admission should be screened for TB.

The prison and remand cell should follow and implement TB infection control guidelines. There is need for active advocacy and sensitization of relevant ministries and departments for the implementation of TB infection control guidelines in the prisons.

Informal settlements (slums)

To reduce TB transmission in the informal settlement, there is need to have adequate sensitization and advocacy on proper ventilation on the existing structures/ housing and practice of cough etiquette. The implementation of community TB infection control guidelines should be emphasized. Screening, contact tracing and treatment interrupter tracking should be highly emphasized in such settings

Learning institutions and security forces training camps

Learning institutions should embrace TB infection control guidelines. TB infection control should be incorporated in the school health program. Learning institutions should adopt and own TB environmental measures and Ultraviolet Germicidal Irradiation (UVGI) among others.

Public services transport

- Matatus, buses and trains
- Air transport

TB infection control guidelines should be implemented in public transport sectors. There should be adequate ventilation by opening windows on both sides of the vehicles or applying mechanized ventilation. Airline services should implement TB Infection control guidelines.

10.7. Infection control and isolation of TB patients

People affected by TB can be subjected to arbitrary and harmful measures such as involuntary treatment, detention, isolation and incarceration.

According to WHO: "Involuntary isolation, except in narrowly defined circumstances (see below for exceptional circumstances and specific conditions that must be met), is unethical and infringes an individual's rights to liberty of movement, freedom of association, and to be free from arbitrary detention. It is unethical to isolate persons with TB if the person is not contagious or if isolation holds no clear public health benefit to the community."

WHO further specifies exceptional circumstances when involuntary isolation can be considered as the last resort for an individual who is:

i) Known to be contagious, refuses effective treatment, and all reasonable measures to ensure adherence have been attempted and proven unsuccessful

ii) Known to be contagious, has agreed to ambulatory treatment, but lacks the capacity to institute infection control in the home, and refuses care at medical facilities

iii) Highly likely to be contagious (based on laboratory evidence) but refuses to undergo assessment of his/her infectious status, while every effort is made to work with the person with TB to establish a treatment plan that meets his needs.

And ALL of the following nine conditions must be met in order to justify any involuntary isolation:

1. Isolation is necessary to prevent the spread of TB
2. Evidence that isolation is likely to be effective in this case
3. Person with TB refuses to remain in isolation despite being adequately informed of the risks, the meaning of being isolated and the reasons for isolation
4. A person with TB's refusal puts others at risk
5. All less restrictive measures have been attempted prior to forcing isolation
6. All other rights and freedoms (such as basic civil liberties) besides that of movement are protected
7. Due process and all relevant appeal mechanisms are in place
8. Person with TB has, at least, basic needs met
9. The isolation time given is the minimum necessary to achieve its goals

10.8. Evaluation of TB infection control measures

Evaluation of TB infection control measures is done by reviewing the medical records of a sample of TB patients seen in the facility. The evaluation of outcome measures can then be used to identify the areas where improvement may be needed. The process of developing and implementing the TB infection control plan is not static, but is a process that should be continually monitored and adapted, with ongoing education integrated at all steps.

Monitoring and Evaluation key areas

Periodic supervision of the measures outlined in the IPC plan.

1. Surveillance of active TB rates among HCWs in the health facility
2. Review medical records of a sample of TB patients seen in the facility to evaluate the following outcome measures;
    - Time interval from admission to suspicion of TB
    - Time interval from suspicion of TB to ordering sputum for AFB smears
    - Time interval from ordering to the collection of sputum
    - Time interval from the examination of the smear to the reporting of results
    - Time interval from the return of laboratory results to the initiation of treatment.

MANAGEMENT OF LATENT TB INFECTIONS

11

Definition of terms

Adolescent: A person aged 10–19 years

Adult: A person over 19 years of age

Bacteriologically confirmed TB: TB diagnosed in a biological specimen by smear microscopy, culture or a WHO-approved molecular test such as Xpert MTB/RIF®

Child: A person under 15 years of age

Contact: Any person who was exposed to a person with tuberculosis

Contact investigation: A systematic process for identifying previously undiagnosed people with TB disease and TB infection among the contacts of an index TB patient and/or other comparable settings where transmission occurs. Contact investigation consists of identification, clinical evaluation and/or testing and provision of appropriate anti-TB therapy (for confirmed TB cases) or TB preventive treatment (for those without TB disease).

Close contact: a person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index case during the 3 months before commencement of the current TB treatment episode.

High TB transmission setting: setting with a high frequency of individuals with undetected or undiagnosed TB disease, or where infectious TB patients are present and there is a high risk of TB transmission. TB patients are most infectious when they are untreated or inadequately treated. Transmission will be increased by aerosol-generating procedures and by the presence of susceptible individuals.

Household contact: A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of current treatment

Index case (index patient) of TB: The initially identified person of any age with new or recurrent TB in a specific household or other comparable setting in which others may have been exposed. An index case is the person on whom a contact investigation is centered but is not necessarily the source case.

Infant: A child under 1 year (12 months) of age

Latent tuberculosis infection (LTBI): A state of persistent immune response to stimulation by M. tuberculosis antigens with no evidence of clinically manifest TB disease. There is no gold standard test for direct identification of M. tuberculosis infection in humans. Most infected people have no signs or symptoms of TB but are at risk for TB disease. This is also at times referred to as TB infection (TBI).

People who use drugs: refers to people who engage in the harmful or hazardous use of psychoactive substances, which could impact negatively on the user's health, social life, resources and legal situation.

Programmatic management of tuberculosis preventive treatment (PMTPT): All coordinated activities by public and private health caregivers and the community aimed at scaling up TB preventive treatment to people who need it.

At risk group: any group of people in which the prevalence or incidence of TB is significantly higher than in the general population.

Systematic screening for active TB: systematic identification of people with presumed TB disease, in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly. Among those screened positive, the diagnosis needs to be established by one or several diagnostic tests and additional clinical assessments, which together have high accuracy.

TB preventive treatment (TPT): Treatment offered to individuals who are considered at risk of developing TB disease, in order to reduce that risk. Also referred to as treatment of TB infection or LTBI treatment.

Tuberculosis (TB): The disease that occurs in someone infected with M. tuberculosis. It is characterized by signs or symptoms of TB disease, or both, and is distinct from tuberculosis infection, which occurs without signs or symptoms of TB. In this document, it is commonly referred to as "active" TB or TB "disease" in order to distinguish it from LTBI or TBI.

Underweight: Among adults this usually refers to a body mass index <18.5 and among children < 10 years to a weight-for-age < −2 z-scores.

Introduction

Latent TB infection (LTBI) is a state of persistent immune response to stimulation by *M. tuberculosis* antigens with no evidence of clinically manifestation of active TB. It is estimated that approximately one-quarter of the world's population (about 1.3 billion people) have LTBI and 5-10% of these are at risk of progression to active TB disease over the course of their lives, most of them within the first 5 years after initial infection.

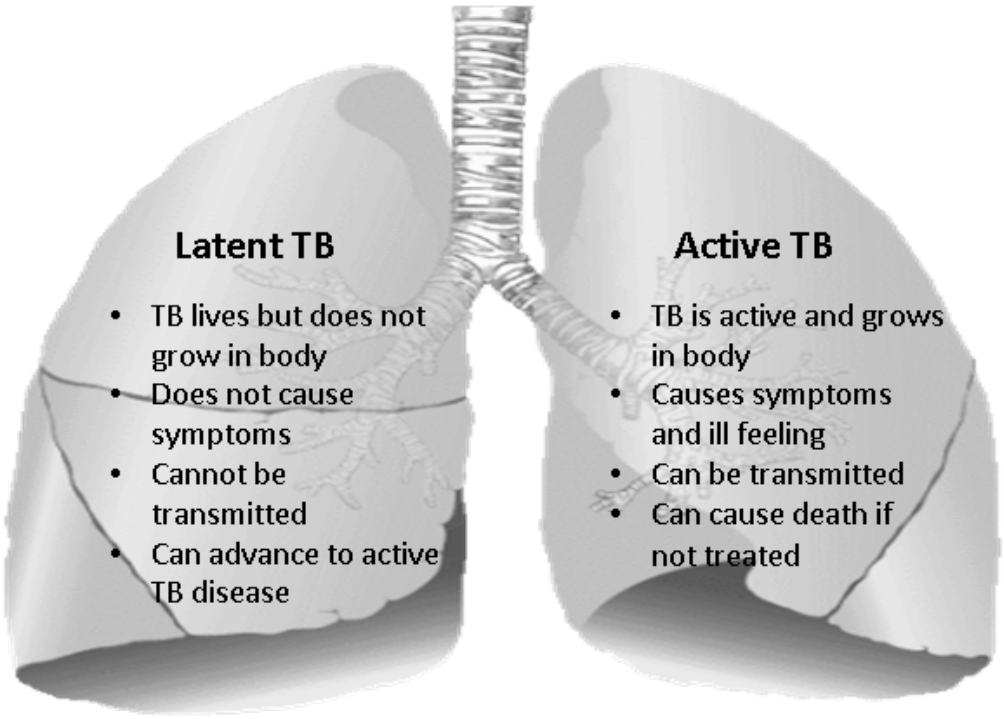
When a person inhales the air that contains droplets with M. tuberculosis bacilli, most of

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. 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 protects the body from foreign substances. At this point, the person has latent TB infection (LTBI).

The risk of progression to active TB disease after infection depends on several factors, the most important being immunological status such as HIV, severe malnutrition, patients on immunosuppressive therapy etc. Provision of TB Preventive Therapy (TPT) has proven itself an effective intervention to avert the development of active TB disease, with efficacy ranging from 60% to 90%.

The World Health Organization's (WHO) 2015 End TB Strategy recognized that people with LTBI are important as they are the "seedbeds" (reservoirs) of active TB disease thus offering TPT will end up lowering the burden of TB.

Table 11.1: Difference between Latent TB Infection and Active TB Disease



Targeted populations for TPT

The following are the targeted populations to be initiated on Tb preventive therapy in Kenya. These populations are vulnerable due to prolonged exposure, compromised immunity, closed confinement and progression to active TB disease.

a. People Living with HIV

b. All household contacts of a person with Bacteriologically confirmed pulmonary TB patients (children, adolescents and adults)
c. Prisoners and Prison staff
d. Health care workers and support staff working in health care settings
e. Others population at risk.
    i. Patients on immunosuppressant's.
    ii. Patients on dialysis
    iii. Patients preparing for an organ or haematological transplant
    iv. Patients with silicosis

NB- The country is not yet recommending TPT for contacts of multidrug-resistant (MDR) or extensively drug-resistant TB.

Risk factors for Latent TB infections

- High prevalence of TB disease in population
- Smear positivity of cases in population (infectivity of cases)
- Type of TB disease
- Proximity and duration with the infectious cases
- Environmental factors e.g poor ventilation, overcrowding
- Immunocompromised patients (HIV, patient on dialysis, diabetic, organ transplant patients, Patient using immunosuppressive drugs)

How to rule out active TB

Rule out active TB using the following screening questions before initiating TB preventive therapy:

- Cough of any duration
- Weight loss/ loss of appetite
- Night sweats
- Fever

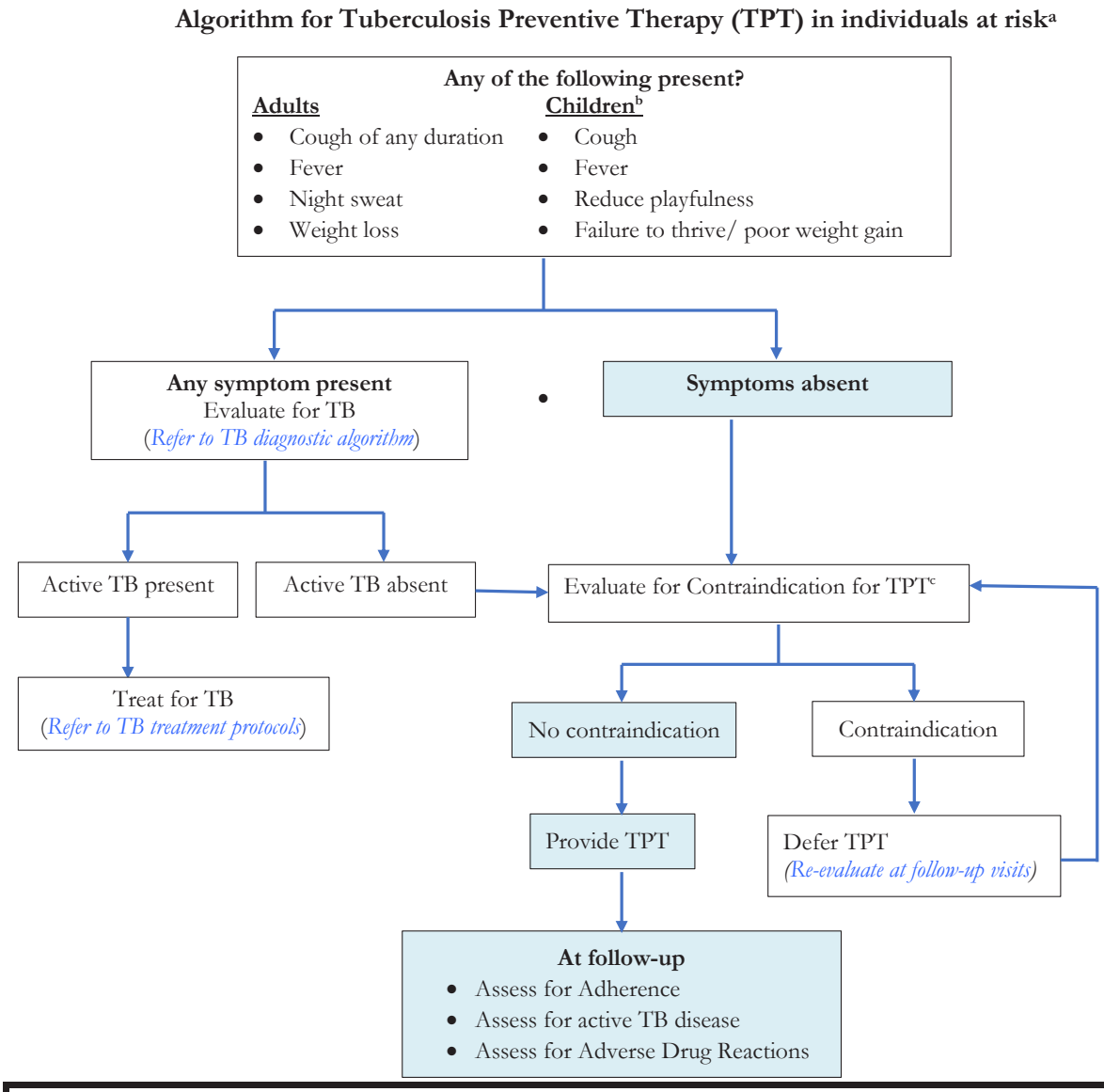
For children also assess for;

- Failure to thrive
- Reduced playfulness/lethargy
- History of contact with a TB patient

NB; Any one presenting with any of the above symptoms should be investigated further to rule out TB disease before initiating TPT.

Algorithm for use before initiating TB Preventive Therapy in the at risk population

Figure 11.1: Algorithm for Tuberculosis Preventive Therapy (TPT) in individuals at risk



TPT Treatment Options			
Age category	**HIV status**	**Treatment Options**	**Frequency[d]**
<15 years	HIV negative	3RH (Rifampicin/Isoniazid)	Daily for 3 months
	HIV positive	6H (Isoniazid)	Daily for 6 months
≥15 years	Regardless of HIV status	3HP (Isoniazid/Rifapentine)	Once weekly for 3 months
If 3HP or 3RH is contraindicated or In Pregnancy		6H	Daily for 6 months
Pyridoxine is given with all of the above options			

Note:

a. Individuals at risk are: PLHIV, household contacts of bacteriologically confirmed pulmonary TB, healthcare workers, prisoners, patients on dialysis, on cancer treatment, undergoing organ or haematological transplant and those with silicosis
b. Child – a person under the age of 10 years
c. Contra-indications for TPT include active hepatitis (*acute or chronic*), symptoms of peripheral neuropathy and chronic alcohol abuse
d. Refer to dosing charts for appropriate dose

LTBI testing by TST or IGRA is not a requirement for initiating TPT in PLHIV and child household contacts aged <5 years. However, it *may* be provided prior to TPT to the rest of the at-risk population if available and does not delay or hinder access to TPT.

Diagnosis and testing of latent TB infections

A diagnosis of latent TB infection is made if a person's medical evaluation does not indicate TB disease. TB disease is first ruled out through medical history, physical examination, chest x-ray, and other laboratory tests.

Testing and diagnosis of Latent TB infections is essential to ensure that we detect the right persons to benefit from TPT thus reducing wastage of resources.

The diagnostic options for Latent TB infections are as follows;

- Tuberculin skin test (TST)
- Interferon-gamma release assays (IGRA)

PLHIVs and children less than five years exposed to bacteriologically confirmed TB patients do not need TST/IGRA before initiating treatment for LTBI

NOTE:

LTBI testing using TST or IGRA, or even assessment with chest radiography is not mandatory and should not be a hindrance for initiating TPT.

TB Preventive Therapy Options

Provision of TB preventive treatment has proven to be an effective intervention to avert the development of active TB disease.

Initiation of TPT

Patient Preparation

Before initiation of TPT, all eligible persons should be subjected to symptom-based screening to rule out active TB and to prevent emergence of antimicrobial resistance (AMR). Persons screening negative for TB and are eligible, should be initiated on appropriate TPT regimen to reduce the risk of progression from LTBI to active TB disease. Other key considerations will include assessment of:

- Signs and symptoms of liver disease such as yellowness of eyes/jaundice, tenderness of the abdomen
- Other comorbidities like diabetes mellitus and associated neuropathy (persistent numbness and burning sensation in the feet and hands).
- Active substance or alcohol use / abuse
- Nutritional assessment (BMI, z score)

Where available; baseline LFT s are recommended for all eligible for TPT. Note that lack of LFT results should not delay the initiation of TPT in asymptomatic patients

If the patient does not have any abnormality based on the assessment above, conduct patient education and assess for adherence using the criteria on the backside of the ICF/ TPT card.

Recommended Treatment Options

There are 3 regimens that can be used as TPT listed below

- Rifapentine/Isoniazid
- Rifampicin/Isoniazid
- Isoniazid

Table 11..2: Recommended regimens for TPT and their indications.

TPT Regimen	Indications	Further considerations
Rifapentine and isoniazid (3HP) Once Weekly for three months (*12 doses*)	• Adult PLHIVs excluding patients on PI-based ARV regimens • All household contacts of Bacteriologically confirmed pulmonary TB patients, who are aged ≥15 years • Health care workers Prisoners and staff in prison settings • Other adult population at risk (e.g., patients undergoing chemotherapy, patients on dialysis, patients undergoing transplant, patients with silicosis)	• There is currently insufficient data to support the use of RPT and INH in pregnancy • Rifapentine can decrease levels of hormonal contraception • INH should not be given to persons with known pre-existing liver damage to avoid an additive effect on liver dysfunction • INH can cause peripheral neuropathy. Vitamin B6 helps prevent peripheral neuropathy
Rifampicin plus Isoniazid (3RH) Daily for 3 Months (*84 doses*)	• HIV negative children aged <15 years who are contacts of Bacteriologically confirmed pulmonary TB patients	
Isoniazid (6H) Daily for 6 months (*168 doses*)	• Adult PLHIV on PI-based ARV regimens • All CLHIV aged below 15 years Any patient with intolerance or contraindication to 3HP or 3RH • Pregnant women	

Note: *All TPT regimens should be offered with pyridoxine. Full patient dose should be available for the entire treatment period before initiating treatment in all regimen.*

DOSING SCHEDULE FOR TPT REGIMENS

A. Daily INH for 6 months (6H)			
Weight (kg)	**Dose (mg)**	**Number of 100mg INH tablets**	**Number of 300mg (Adult) tablet**
<5	50	½ tablet	-
5.1-9.9	100	1 tablet	-
10-13.9	150	1 ½ tablet or	½ tablet
14-19.9	200	2 tablets	-
20-24.9	250	2 ½ tablet	-
≥25	300	3 tablets or	1 tablet
Adult	300	3 tablets or	1 tablet
Note: Syrup INH (50mg/5ml) is available for younger children			

B1. Daily RH for 3 months (3RH) for children <25kgs		
Weight (kg)	**Number of tablets (RH 75/50mg)**	**How to reconstitute the medicine**
Less than 2	¼	Dissolve one (1) tablet of RH in 20 ml of safe drinking water. Once fully dissolved, give 5ml (1/4) of this solution measured with a syringe.
2 – 2.9	½	Dissolve one (1) tablet of RH in 20 ml of safe drinking water. Once fully dissolved, give 10ml (1/2) of this solution measured with a syringe.
3 – 3.9	¾	Dissolve one (1) tablet of RH in 20 ml of safe drinking water. Once fully dissolved, give 15ml (3/4) of this solution measured with a syringe.
After giving the child their dose for that day, discard the rest of the solution. Prepare a fresh solution every day.		
4-7.9	1	Dissolve the tablet(s) of RH in 20mls of safe drinking water. Once fully dissolved, give ALL this solution to the child
8-11.9	2	
12-15.9	3	
16-24.9	4	

B2. Daily RH for 3 months (3RH) for children ≥25kgs (To use Adult formulation)	
Weight (kg)	**Number of tablets (RH 150/75 mg)**
25-39.9	2
40-54.9	3
55kg and above	4

C. Weekly 3HP (3HP) (For adults and adolescents ≥15 years)	
3HP products	**No of Tablets**
Rifapentine 150mg tabs	6
Isoniazid 300 mg tabs	3
Rifapentine 300mg+Isoniazid 300mg (FDC)	3

D. Dosage of Pyridoxine (Vitamin B6)			
Weight (kgs)	**Dosage in mg**	**Number of 25mg tablets**	**Number of 50mg tablets**
<5	6.25 mg	½ Tablet 3 times a week, alternate days	-
5.0-7.9	12.5 mg	Half a tablet	-
8.0-14.9	25 mg	One tablet	Half of 50mg tablet
15kg and above	50 mg	Two tablets	One 50mg tablet
Adults	50 mg	Two tablets	One 50mg tablet

Follow Up of Patients on TB Preventive Therapy (TPT)

Patients on TPT should be followed up on a monthly basis and clinic harmonized with any other routine clinic schedule. During each clinic visit, conduct the following;

- Conduct symptom based TB screening at every clinic visit for patients on TPT and update TB status
- Assess and reinforce adherence of the patients at every visit to ascertain compliance and completion of doses
- If a patient tests positive for TB while on TPT, stop TPT and initiate TB treatment

Assess for any adverse drug reactions at each visit and intervene appropriately

Management of Drug toxicities

(i) Peripheral neuropathy

May be potentiated by other neurotoxic drugs, alcoholism, metabolic disease (diabetes), malnutrition and infections

Rarely severe enough to require drug withdrawal

Preventable with low dose supplemental pyridoxine (Table 4)

Treated with high dose pyridoxine (25-50mg/day)

Relief of symptoms- Give any of these Analgesics, Tricyclic antidepressants (amitriptyline, nortriptyline) Anticonvulsants (carbamazepine, phenytoin)

(ii) Drug induced hepatitis

Elevation of liver enzymes may occur in the first weeks of treatment.

Serum liver enzyme levels do not need to be monitored routinely, as asymptomatic mild elevation of serum liver enzymes (less than five times the normal values) is not an indication to stop treatment

All clients with gastrointestinal symptoms (nausea and vomiting, liver tenderness, hepatomegaly or jaundice) should have their liver function assessed

Grading and management of Hepatitis

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
ALT (SGPT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
AST (SGOT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
ACTION	Continue treatment regimen; Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	Continue treatment regimen; Patients should be followed until resolution (return to baseline) or stabilization of AST/ALT elevation.	Stop all drugs, including TPT drugs; Measure LFTs weekly; Treatment may be reintroduced after toxicity is resolved.	Stop all drugs, including TPT drugs; Measure LFTs weekly. Treatment may be reintroduced after toxicity is resolved

Advise patient to return immediately if they develop complaints relating to ADRs as captured above

Assess for patient adherence to medication and emphasize on the importance of adherence during clinic visits.

Screen for active TB during each clinic visit using symptom based on TPT card/ tool.

Update the TPT record cards and the TPT register at every visit and document the outcome on completion of therapy

Contraindications for TPT

(i) Active TB disease

(ii) Signs and symptoms of hepatitis (Jaundice, elevated liver enzymes)

(iii) Symptoms of peripheral neuropathy. In adults and older children; persistent numbness, tingling or burning sensation, in limbs. In younger children; regression in motor milestones, refusal to crawl, walk or run.

Note: If the client has any of the above contraindications, defer TPT and manage underlying cause.

Defer TPT in cases of the following scenarios;

Contraindications, abnormal Chest X Ray, Active substance abuse, History of poor adherence.

Defer and manage the underlying condition and re-evaluate for TPT in the next visit.

Note: History of TB and current pregnancy is not a contraindication for starting TB preventive treatment.

Managing interruptions for TPT

Scenario	Action
1. For a client initiated on TPT and discontinues for any reason within the first 4 weeks 2. For a client on TPT for more than 28 days and subsequently misses TPT doses for more than 2 weeks	• Conduct adherence counselling • Address reasons for interruptions • Screen for active TB and if asymptomatic **restart TPT** • Ensure they have completed a full course of treatment • For the weekly doses, take the missed dose as soon as they remember
3. For a client on TPT for more than 28 days and subsequently misses TPT doses for less than 2 weeks (<28 days)	• Conduct adherence counselling • Address reasons for TPT interruption • Screen for active TB and if asymptomatic **continue with TPT** and compensate for the duration doses were missed • Ensure they have completed a full course as per the national guidelines
4. For a client with maximum two TPT interruptions	• Do not re-initiate on TPT

TPT Outcomes

Treatment Completed: An individual who has taken a full course of LTBI treatment in line with the guidelines

Treatment not completed: An individual who did not take a full course of LTBI treatment.

Failure to complete treatment could be due to:

a) **Lost to follow up** – An individual whose LTBI treatment was interrupted for more than one month

b) **Discontinued** –An individual whose LTBI treatment was discontinued due to;

ADR - Adverse drug reactions

TB - Develop active TB disease in the course of treatment

c) **Died** - An individual who died in the course of LTBI treatment

Follow up after completion of TPT

- Conduct symptom-based TB screening at every clinic visit for patients who have completed TPT at 6 and 12month (from TPT completion) and TB status for every patient in the TPT register
- If a patient screens positive after completing TPT, manage according to national TB guidelines.

TPT Adherence

Adherence

Adherence refers to the degree to which a client follows an agreed course of treatment as recommended by a healthcare provider.

Optimizing adherence

Once clients have been initiated on TPT, health care workers need to monitor patient progress and provide information on

- the usefulness of TPT
- importance of completing treatment
- any anticipated side effects and toxicities

Barriers to treatment adherence can arise from the following factors.

- Client
- Social influence
- Health system
- Medication
- Clinical

What are some of the key interventions in reducing the non-adherence to treatment?

- Ensure the patient has adequate information regarding TPT
- Ensure a good treatment plan between the client and the facility
- Ensure any side effects are detected early and managed
- Adapt available social support mechanisms
- Utilization of Innovative health communication, use of digital health platform

What should the national and county level do to Improve TPT adherence

Policy makers	Health care workers	Clients
Health systems: strengthen health systems to ensure availability and accessibility of diagnostic services for LTBI treatment and care	Empowerment: a). Build the capacity of the health care workers to understand LTBI, diagnosis, regimens, efficacy, possible side effects and the risks b). Train healthcare workers on Human Rights and stigma and discrimination reduction	Develop health Education package for clients on LTBI: Importance of taking the treatment and completing Anti-Stigma campaigns Train on myths and misconceptions of LTBI
Develop, print and disseminate policies / guidelines Avail both hard and soft copies (websites)	Develop health Education package on LTBI: treatment for clients on diagnosis, regimens, efficacy, benefits, possible side effects and the risks and on Importance of taking the treatment and completing Anti-Stigma campaigns Train on myths and misconceptions of LTBI	Educate the clients on the use of technology to facilitate / promote adherence Initiate mini groups on treatment adherence Develop Reminders messages for patients Make a calendar or pill box for the client
Advocate for Increase budgetary / resources allocation to facilitate engage of more health workers in service delivery	Ensure availability of guidelines, algorithm from the national levels at the county, Sub- County levels and facility level	Involve patient in treatment plan: Patients centered interventions: One to one Education/Counseling offering the available options
Provide mentorship, counselling and on the job training on the health care workers	Use of alarm, SMS Family members support as reminders for treatment adherence	Agree on verbal consents for treatment
Develop, print and distribute IEC / promotional materials Develop social media materials for mass campaign	Promote Community support groups at the health facilities to offer psycho social support	
Implement rights based approach LTBI treatment and care		
Improve health cares system to ensure access and affordability		

Roles of health care workers and clients to improve TPT adherence

Health care Providers	Client
Educate patients/clients on LTBI: treatment education for clients (diagnosis, regimens, efficacy, benefits, possible side effects and the risks) on the importance of taking the treatment and completing Anti-Stigma campaigns Train on myths and misconceptions of LTBI	patient/client should ask and agree with the health provider on treatment plan
Sensitize the public on demand for LTBI treatment and care	Report any side effect or reaction to the health care provider
Use of alarm, SMS, Family members support as reminders for treatment adherence	Follow the treatment plan and take medication as instructed by health care provider
Promote Community support groups at the health facilities to offer psycho social support	Participate in patient support mini group
Counselling	Demand for one to one counselling session with the health care provider
Have high index of suspicion to rule out Active TB	Request for TB screening
Order for a repeat X ray if the patient develop signs /symptoms suggestive of TB disease	
Carry out periodic assessment of treatment adherence	Participate in periodic adherence assessment
Provide Post treatment follow up	Report any abnormal condition, signs and symptoms to the health care provider
Carry out continuous education to clients on TPT	
Document and keep the records of TST and IGRA results and other medical records for the clients on treatment and after treatment	Keep records of all documents on testing and treatment provided by the health care provider

Monitoring and Evaluation

Monitoring is the routine tracking of service and program performance. It is a continuous process intended to provide information on the extent to which a program is achieving its intended targets within specified time frames. It involves actual recording and reporting processes using standard tools (*as described below and annexed in these guidelines)*.

Recording and Reporting Tools

Recording tools

All facilities should have the following tools either in paper or electronic form:

1. TPT/ Contact management register
2. TPT Appointment card
3. TPT/ICF Patient record card
4. Daily activity drugs register (DADR)
5. Facility consumption data report and request form (FCDRR).

Reporting tools

1. KHIS- MOH 731, FMAPS (729B)
2. TIBU (Case finding form and Cohort analysis form)

The TPT/ Contact management register

This register is used to capture all clients put on TPT regardless of their HIV status. It also serves as the contact management register thus capturing the details of the index case whenever appropriate. Depending on the setting at the facility, it is advisable to place this register in all relevant service delivery points. Health care workers handling this register are advised to go through the instructions on how to fill this register

TPT appointment card

This card is issued to the client upon initiation of TPT. It contains the client's demographic details, a brief on the clinical information and the clinic schedule. The client should be advised to present this card every time they are visiting a health facility for review and/ or drugs collection.

TPT/ ICF Patient record card

This card serves as the client's file as it contains all details of the patient from the time TPT is initiated to its completion. All clinical details related to the client while on TPT should be well captured.

Daily activity drug register

This register captures drugs transactions and regimens dispensed to clients on a specified clinic date.

Facility consumption data report and request form

This is a monthly data capturing tool that summarizes consumption, reporting and ordering of commodities for the health facility.

Reporting tools

Data from the CCC shall be reported on the MOH 731 tool and entered on KHIS on monthly basis while that from all other clinics shall be entered in TIBU by the sub-county TB and Leprosy coordinator on a monthly basis. FMAPs(729B) summarizes patients on TPT regimen among PLHIV.

NOTE:

Every health care provider involved in TB treatment or prevention has a professional responsibility to record and report people treated for TB (latent or active TB)

TB is a notifiable disease under the Public Health Act Cap 242, and therefore all those treated (by the public or private sector) must be notified to the MOH.

DIFFERENTIATED APPROACH TO TB CONTROL

12

12.1 Introduction

TB patient needs are not homogeneous, it is therefore important to design interventions for TB control that are patient-specific and speak to the individual patient needs. The End-TB strategy recommends integrated, patient centered care with bold policies and supportive health systems. Differentiated care for TB is an innovative way of organizing patient care that includes all services aimed at identifying, diagnosing, treating and supporting people in need of TB services. This is also sometimes called tiered care, patient-centered care or patient-tailored care. This approach provides individualized care based on the patient needs that enhances client experience, by co-creating solutions with the patient.

12.2 Problem statement

Tuberculosis (TB) is a chronic infectious disease caused by various species of the *Mycobacterium* genus. If untreated, an infected patient can infect an average of 10-15 persons in a year. Globally, an estimated 10.0 million (range, 9.0–11.1 million) people fell ill with TB in 2019. There were an estimated 251 000 deaths among HIV positive people. TB affects people of both sexes in all age groups but the highest burden is in men (aged 15 years and over), who accounted for 65% of all TB cases in 2018. By comparison, women accounted for 25% and children (under 15 years of age) for 9.7%.

KEY HIGHLIGHTS:

- **Differentiated care aims to provide patient-centred TB care and prevention services while improving efficiencies in the health system**
- **All persons receiving TB services should be profiled at baseline and at each visit to determine eligibility for differentiated care**
- **Patients receiving care under the differentiated approach must adhere to the TB monitoring and follow up schedules to ensure quality of care.**
- **Options for TB services for Key populations have been organized around their needs, and the capacity of the health system to provide client centered services.**

In 2019, there were an estimated 147,000 new TB cases in Kenya. A total number of 86 385 TB cases were notified in the year (59% case detection rate) with a Treatment success rate (TSR) for drug susceptible TB patients of 84% among the 2017 cohort. This was mostly attributed to death rate of 6.3% and loss to follow-up rate of 5.4%.

Interruption of treatment has been a major obstacle to treatment adherence, and is an important challenge in TB control. Inability to complete the prescribed 6-month regimen is an important cause of treatment failure, relapse, acquired drug resistance and on-going transmission of infection. Treatment interruption is a precursor to loss to follow up which therefore provides an opportunity for early intervention in the course of treatment to prevent treatment interruption.

Risk factors for treatment interruption include:

- Long transportation time to health facilities
- Male gender
- Patients with low level of information about TB, inadequate education and counselling on TB
- Poor quality of communication between patients and health workers,
- Long distances to treatment centres,
- Inadequate knowledge of TB treatment duration and possible adverse effects of anti-TB medication.

12.3 Justification

The rate of treatment interruption was highest during the initial two months (the intensive phase of treatment). Enhanced patient pre-treatment counseling and education about TB is key in the reduction of loss to follow up and deaths due to inadequate quality of TB care. (Adherence study, Kimuu)

Differentiated service delivery, also known as differentiated care, is a client-centered approach that simplifies and adapts TB services to reflect the preferences and expectations of various groups of people diagnosed with TB while reducing unnecessary burdens on the health system. By providing differentiated service delivery, the health system can reallocate resources to those most in need. (Differentiated Care Toolkit, Global Fund)

Differentiated service delivery aims to enhance the quality of the client experience. It puts the client at the centre of service delivery. It also ensures the health system functions in both a medically accountable and efficient manner.

12.4 Objectives of differentiated care in Tuberculosis management

Differentiated care aims to:

- Enhance the quality of the patient experience.
- Put the patient at the Centre of service delivery.
- Ensure that the health system functions efficiently.

Under a differentiated approach, patients are profiled based on;

- Clinical status i.e. stable/ unstable based on disease severity, comorbid conditions e.g. HIV, Diabetes, malnutrition, sputum conversion, nutritional status and adherence to treatment.
- Psychosocial and socioeconomic status-employment status, presence of social support, homeless and street families
- Patient demographics - Men, the elderly, adolescents, young children, refugees, mobile populations, vulnerable groups such as PWIDs, alcoholics, health care workers, people in congregate settings and contacts of bacteriologically confirmed pulmonary TB.

12.5 Modules in Differentiated Care

There are three modules in provision of differentiated care:

- Differentiated screening and testing for TB
- Differentiated TB treatment and care
- Differentiated drug delivery for TB.

1. Differentiated screening & testing for TB

Differentiated screening and testing approaches are based on the preferences of targeted groups, the cost of service delivery, and the expected testing efficiency. Available options include Active TB case finding in health facilities, targeted screening for TB in at risk groups in hotspots and integrated community screening and testing

Typical population groups that may benefit from integrated TB screening and testing include:

- HIV clients who are potentially co-infected with TB: integration of TB screening and testing with HIV testing
- Infants and children: Targeted TB screening and testing during immunization

- Pregnant women, new mothers and infants: Screening and testing for TB during ANC visits, Child welfare clinics and mother and child health outreaches
- Rural communities living in remote areas: Screening and testing for TB alongside other primary care services
- Injecting drug users: integrating TB screening and testing with methadone assisted therapy (MAT) clinics, drop-in centers(DiCES), and harm reduction outreach services
- Men: offering TB screening and testing in workplaces, during community health campaigns, in locations such as social places or bars where men are more likely to attend.
- Health care workers: Bi-annual screening and testing for TB for all health care workers integrated in world TB day and World AIDS day celebration activities.
- Adolescent: Targeted TB screening and testing in learning institutions, Integrating TB screening and testing in youth friendly clinics and programs
- Contacts of bacteriologically confirmed pulmonary TB: Community based contact screening and testing
- The elderly: Integration of TB screening and testing with existing social support mechanisms e.g. The older person's cash transfer

2. Differentiated treatment & care

12.5.1 Introduction

Differentiated treatment and care approaches are most applicable to facilities that have a high volume of patients and provide all health services. The approaches increase cost-efficiency by optimizing staff workload. They further improve health outcomes for patients through higher adherence to treatment and retention in care through the combined effects of targeted counseling, peer support, reduced waiting times and reduced congestion at the facility.

Design of approaches should start from what is known about patient perspectives on existing arrangements for services and the proposed new models of service delivery. Community and patient engagement is vital to bring meaningful improvements in services.

To identify options for differentiated treatment and care, the following questions will be considered;

a) What needs do TB patients require regarding treatment and care?

This will involve evaluation of the patients':

- Demographics - Men, the elderly, adolescents/ young children
- Vulnerability - PWID, Health care workers, alcoholism, refugees
- Health conditions - co morbid conditions e.g HIV, Diabetes, Pregnancy etc

b) What barriers do patients and health care workers face?

Patient-related barriers

- Access to health services - Physical constraints such as disability, inflexible hospital working hours, long hospital waiting time.
- Poor organization of health services e.g. overcrowding in waiting bays, lack of confidentiality, long waiting times, frequent hospital appointments and stigma by community members
- Patient specific needs e.g boarding school attending adolescents, university students, employee working hours

Health care worker - related barriers

- Inadequate capacity to offer quality TB services e.g inadequate training, lack of relevant equipment, lack of job aids and tools.
- Inadequate clinic space for TB service provision
- Lack of consumption of data for decision making

c) What are the available opportunities in TB treatment and care?

Opportunities for task shifting- TB services can be administered by various cadres in health care service provision such as- doctors, clinical officers, nurses and community health workers.

Opportunities for capacity building of health care workers through formal training, ECHO.

Opportunities for integration of TB treatment with service delivery points e.g. Comprehensive care clinic, Maternal and child health services, nutrition services, inpatient services, learning institutions and other areas such as workplaces

d) Is the facility serving large numbers of patients?

What are the issues experienced in high volume facilities?

- **For patients**- longer waiting time, delay in service provision in the various service delivery points, increased risk of infection transmission, inadequate contact with health workers during consultation.
- **For health care workers**- High potential for burn out due to high workload, are at high risk of contracting infection, compromised quality of care.

12.5.2 What are some of the options available in differentiated treatment and care?

a. Having differentiated appointment schedules

Health facilities can dedicate specific clinic days with flexible appointment schedules and opening hours to specific patient groups based on their clinical, demographic and psychosocial needs.

b. Having differentiated clinical management plans

Health facilities require specific management plans for specific patient groups e.g. children and adolescents, drug resistant TB patients, TB/HIV co-infected patients, TB/DM patients and so forth.

c. Design of differentiated patient flow

Health facilities can designate specific pathways for specific groups of patients e.g. smear positive versus smear negative and stable patients versus unstable patients.

12.5.3 Differentiated TB drug delivery

Differentiated drug delivery includes dispensing drugs to patients as well as ensuring continuous, reliable and quality supplies of drugs and other commodities for treatment and care.

Differentiated drug delivery approaches offer specific and cost-effective opportunities to innovate. They can differ to match the needs and preferences of specific patient groups.

The following questions will guide the identification of opportunities in differentiated drug delivery

a) What is the profile of patients in my facility?

All TB patients should be evaluated for eligibility to receive differentiated care. Profiling, however, should continue during every clinic visit as a patient's status may change during treatment. Profiling is conducted using several parameters that identify a patient as either stable or unstable. These Include;

1. History of Previous TB treatment
2. Clinical Presentation
3. Presence of comorbidities
4. Pregnancy
5. Adherence status
6. Demographic groups
7. Gender
8. Drug Resistance Pattern

b) What barriers are patients and health service providers facing in drug delivery?

i. Patient barriers

- Physical barriers to access for drug refills (distance to the facility, difficult travel conditions, poor availability of drugs);
- Time and cost constraints (e.g. remote location, constraining work hours, travel cost, loss of income while accessing health services, long waiting times);
- Stigma from community, family or service provider during drug refill visits (e.g. lack of privacy, confidentiality or respect);
- Lack of treatment support from peers, community or family.

ii. Health service provider barriers

- High volume of clients at the facility, leading to congestion and lengthy waiting times for clinical appointments and at the pharmacy;
- Lack of human resources for pharmacy management and dispensing

c) What are the opportunities to adjust the current service-delivery model?

Health facilities should develop service delivery models that best address patient needs and constraints, while working around the constraints of service providers, potentially offering several combination options to clients.

Any service delivery model is a combination of three factors, each of which has potential for adjustment:

- **Who provides the service** – e.g. doctors, clinical officers nurses and community health workers
- **Where the service is provided** – at various points in the health centers (regional and district hospitals, health centers, dispensaries, etc) vs. distribution points in communities or at home;
- **How often the service is provided** – Facilities can vary the frequency of visits, type of service provider, or service location to improve patient satisfaction. These should improve case holding in care and better outcomes are observed.

12.5.4 Available options for differentiated drug delivery

1. Appointment spacing

Appointment spacing is an approach that can be applied based on whether the patient is stable, distance to facility, number of patients served by the facility.

For stable patients' appointment should be spaced 2 weekly in the intensive phase and monthly in the continuation phase.

2. **Fast-tracking drug refills**

   Facilities can adapt the patient' pathways, based on the purpose of their visit and eligibility to skip a few steps of the process. For example, stable TB patients with good adherence record could be "fast-tracked" and access the pharmacy directly for refills. Alternatively, to fast track drug refills, pre-packed drugs can be done for stable patients.

3. **Decentralized drug delivery in communities**

   For stable and adherent patients living in remote areas where distances to facilities are far, drugs should be given to patients for a longer duration for example one month in the continuation phase or to community health volunteers who act as treatment supporter for mobile populations. Appropriate and proper adherence counselling and patient education is required to mitigate loss from care and treatment as well as identification of indicators of poor treatment outcomes such as adverse drug reactions. Linkage to their nearest health facility is also required should the patient require any support.

12.6 Differentiated Care Approaches for TB Key Populations

The Kenya National TB Strategic Plan 2019-2023 identifies key patient groups for TB control. These groups were identified following a rigorous review process of current epidemiological data in the country. Additionally, the needs of these groups are unique and depend on the local context. As such, differentiated approaches should take these into consideration during the design and implementation stages.

1. Men

Screening and testing

- Offer integrated, out of facility TB screening and testing in workplaces, social places e.g. entertainment spots.
- Active case finding for TB in health facilities must engage men to ensure linkage to testing

Treatment and care

All effort must be made to engage with the patient to determine which model of care works best to ensure their adherence, based on the patient's profile. These solutions include;

- Clinic visits can be made without the need to miss work engagements
- Longer appointments -2 weekly in intensive and monthly in the continuation.
- Calling the facility in case of any concern rather than physically visiting a health facility.
- Integration of required services to provide a one-stop shop experience.

Drug delivery model

Restructure patient flow to ensure minimum time spent within health facilities for all stable patients

- Where clinic visits interfere with work timings, consider drug collection outside clinic timings where necessary.
- Fast-track drug refills for stable, adherent patients
- Consider pre-packing patient medicines, prior to the clinic date
- Consider longer refill dates for stable patients Community volunteers can support in delivering drug refills within the community where feasible

2. Adolescents and youth (10-24 year olds)

Adolescents and youth are a special patient group with specific physical needs that require addressing, notwithstanding evolving emotional and physical changes. Majority of adolescents and youth in Kenya attend boarding schools and institutions of learning, while many others though in day schools, may be uncomfortable to attend the same clinics as adults due to stigma. Additionally, institutions of learning are mostly overcrowded and have a higher risk of TB infection transmission.

Screening and testing

Out of facility TB screening and testing for adolescents and youth should be integrated into the school health programs, institutions of learning and other social settings that adolescents and the youth frequent. These include;

- Schools and institutions of learning, particularly where a TB patient has been identified in an institution.
- Church groups,
- Sports and holiday camps
- Sports activities.

Treatment and care

All health facilities should attempt to provide youth-friendly services where adolescents and the youth can feel comfortable, and well supported towards treatment adherence. An environment where adolescents can ask questions regarding their care and other issues affecting them must be created. This support can be provided through;

- Peer support groups at facility level
- Adolescent or youth peer educators at facility level who counsel, and provide health education
- Youth specific clinic days where only adolescents and the youth are attended to particularly in large health facilities.

- Thorough evaluation of identification of contacts to ensure contact invitation and management is conducted to reduce the risk of transmission

Drug delivery model

While the majority of adolescents and the youth attend institutions of learning such as boarding and high schools, technical institutions and colleges, all effort must be made to ensure there is no interruption of these key activities due to the disease or clinic attendance. Suggestions for drug models for this group include;

- Aligning clinic visits and drug refills to holidays
- Where necessary engaging school nurses and institutional clinics as DOT providers

3. Infants and Children below 10 years

Children below 10 years of age have unique needs and are considered unstable patients. However, specific interventions can be tailor-made to facilitate case finding and management of TB in this patient group as shown below:

Screening and testing

- Facility Targeted TB screening during scheduled immunization and nutritional review clinics.
- Targeted screening in boarding schools and enhanced linkage to the school health program.

Treatment and care

- Integrated TB treatment at Maternal and Child health services/nutrition services where applicable.
- Have specific clinic days for infants and children, where differentiated management plans and reviews can be done for the age group.

Drug delivery model

Children and infants are considered unstable patients and should follow the weekly scheduled appointments in the intensive phase and the fortnightly appointment in the continuation phase for drug sensitive TB while for Drug resistant TB should be directly observed therapy.

4. People who inject drugs

People who inject drugs are recognized as a high risk group for TB transmission and non-adherence to treatment.

Screening and testing

- All attempts must be made to screen people who inject drugs for TB within their natural and congregate settings which include Methadone Assisted Therapy (MAT) clinics and Drop in centers (DiCES).
- TB screening should be integrated into all services given to people who inject drugs.

Treatment and care

- People who inject drugs are considered unstable patients and their clinic schedule should be daily.
- Differentiated management plan which include nutritional support, psycho-social counselling and any other specific support required by the PWID should be integrated.

Drug delivery model

Drug delivery for people who inject drugs should be as directly observed therapy and should be integrated into the methadone administration schedule or as they come for their daily support at the Drop in centres.

5. Health workers

Healthcare workers (HCWs) have a two- to three-fold increased risk of developing TB compared with the general population due to frequent and prolonged exposure to undiagnosed persons with TB or DRTB in the workplace. It is also estimated that in some sub-Saharan countries the rate of HIV in HCWs is approximate to the rate in the general population, placing these HCWs at an even greater risk of developing TB. In many low-resourced settings, there are limited infection control measures in place to protect HCWs in the workplace. HCWS should know their HIV status and be provided ART and IPT to prevent TB, and all HCWs should be screened regularly for TB and adhere to infection prevention and control measures.

Screening and testing

- Due to the high risk of developing TB, health workers need to be screened for TB at least twice a year. Integration of health worker screening into existing national celebrations e.g as a build up to World TB day celebrations and World AIDS day celebrations. (Refer to SoP on health worker screening)
- Routine screening and testing for TB should be done any time a health worker has any symptoms.
- All HCWs with presumptive TB must be tested using GeneXpert, which will also give information on drug susceptibility to rifampicin.

Treatment and care

- Where possible, health facilities should dedicate specific clinic days for health workers with TB, with flexible appointment schedules and opening hours to suit their needs.
- Health facilities require specific management plans for health workers. This may involve operationalization of staff clinics with integrated management of health worker related issues be they mental health, physical health and substance abuse.

Drug delivery model

- Drug refills for all stable HCWs seeking treatment should be fast tracked to reduce time spent seeking care. In addition, the patient pathway followed by this category of patient may be modified to have drug refills done directly at the pharmacy or other dispensing point without necessarily passing through the clinical areas. This will reduce infection transmission as well as enhance client experience.
- Appointments for drug refills for health workers may also be spaced to reduce frequency of clinic visits.

6. Rural communities

Persons living in rural communities face unique challenges in accessing TB care due to long distances to health facilities, inadequate access to TB services and financial challenges hence requiring cost cutting measures to ensure treatment access. The following are key considerations and options for this populations.

Screening and testing options

- Targeted screening during market days
- Integration of TB screening with other outreach services.
- Any other context-specific option as per their location

Treatment and care

- For stable patients in rural communities, appointment schedules may be extended to have longer intervals between clinical visits.

Drug delivery model

- Engagement of community health volunteers (CHVs) to deliver medicines to stable patients in rural communities.
- Drug doses may be given in higher quantities to facilitate longer appointment schedules

7. People living in urban informal settlements

The National TB Prevalence Survey reported a higher burden of TB in urban (760 per 100,000 population) compared to rural settings (453 per 100,000 population), this is consistent with routine TB data which shows higher notification rates in the major cities. To ensure that these persons receive appropriate TB care services, the following options may be explored

Screening and testing

Out of facility Targeted TB screening which includes;

- Periodic door to door TB Screening
- Integration of TB screening with other outreach services
- Screening for TB within hot-spots in informal settlements.
- Strengthened contact management through community health workers.

Treatment and care

People who live in the urban informal settlement should also be assessed based on demographics (e.g men), comorbidities and vulnerability such as PWID.

Based on this they can have:

- Differentiated clinic Schedules-Flexible appointments schedules, longer spacing of appointments for stable patients (2 weeks in the intensive and a month in the continuation phase).
- Differentiated management plan- Each category of patients group should have a tailored management plan which caters for all the needs of the group such as specific clinics for children, men, patients with comorbidities and adolescents.

Drug delivery model

- Variable clinic appointment spacing for stable patients based on their needs
- Fast tracking drug refills for stable patients to reduce time spent in the health facilities. Drugs can be pre-packed in advance.
- Use of community health workers for drug delivery and as treatment supporters where applicable.

8. People in congregate settings

TB in congregate settings is an area of focus to reach key groups in schools, work places, prisons, refugee camps

Screening and testing

- Regular symptom screening in large workplaces/ industries, schools, universities and other educational institutions.

  Integration of TB in the workplace occupational health systems

  Regular screening of prisoners using the PF-10 form

  Linkage with the formal health system for sample transport and results relay

  Close management of contacts in collaboration with the TB program through County and Sub-County TB coordinators

Treatment and care

Based on patients' assessments and needs, they can have the following

Scheduled appointments -Students who are in schools, universities and workers their timings vary and need scheduled appointments based on availability.

Workers in corporate settings should ideally receive care in an ethical and acceptable setting, ideally, within the workplace occupational health set-up

Flexible appointment timing to prevent loss of man-hours at work and schools

Differentiated management plan to suit the adolescent and young adult group- to have specific clinics for youth which are youth friendly and cater for their needs holistically.

Drug delivery model

Based on patients' assessment and needs, they can have differentiated drug model below;

Appointment spacing- have longer appointments for stable patients.

Fast -track refilling of drugs for stable patients, pre-pack drugs in advance.

Decentralization of drug delivery to schools, universities and workplace where we have health providers/ minder that can provide direct observation therapy.

9. Mobile populations (nomadic communities)

Screening and testing

Targeted community screening at identified kraals in collaboration with kraal leadership

Integrate TB screening within outreach services in the

Contact tracing

Treatment and care

Appointment spacing-longer appointment times for stable patients

Strengthening establishment of TB isolation facilities ('manyattas') in arid areas for those willing to stay for the duration of treatment-ideal

Drug delivery model

Fast tracking during clinic visits for those receiveing care in formal health institutions

Community decentralized model- Use of community volunteers for drug delivery and as treatment supporter where applicable

10. Street Families

Screening and Testing

Targeted screening in 'bases' where the families stay.

Treatment and Care

Using the head of 'bases' for street families as DOT supporters and for follow up.

Nutritional support at the facility for patients

They should follow the standard treatment appointment schedule by the program since they fall in the category of unstable patients

Drug Delivery Model

Pre-packing of drugs and fast tracking for those with no issues.

CHRONIC LUNG DISEASES

13

Introduction

Respiratory diseases account for more than 10% of all disability-adjusted life years (DALYs) and make up five of the thirty most common causes of death. In Kenya, respiratory diseases account for at least 25% of the outpatient morbidity and are among the five highest causes of mortality. Respiratory diseases are an important cause of morbidity and mortality. 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.

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.

This chapter focuses on the following Chronic Lung Diseases:

1. Asthma
2. Chronic Obstructive Pulmonary Disease
3. Post Tuberculosis Lung Disease
    a. Lung scarring (fibrosis)
    b. Bronchiectasis
    c. Chronic Obstructive Pulmonary Disease (COPD)
    d. Lung abscess
    e. Aspergillus-related lung disease
    f. Spontaneous Pneumothorax
4. Interstitial lung diseases
5. Lung cancer

Table 13.1: Causes of chronic cough

Causes of chronic cough	

• **Upper airway:**
  • Upper airway cough syndrome (formerly postnasal drip)
  • Chronic allergic rhinitis
• **Lower respiratory tract causes:**
  • Infections-Tuberculosis, Bronchiectasis
  • Inflammatory-Asthma, Chronic Obstructive Pulmonary Disease (COPD)
  • Autoimmune- Sarcoidosis, Interstitial Lung diseases
	• **Carcinomas-Lung cancer**
	• **Pneumoconiosis**
	• **Cardiac causes: Left heart failure**
	Others:
	  • Gastroesophageal reflux (GERD)
	  • Side effects of certain medicines e.g. ACE inhibitors e.g. Enalapril

13.1 Asthma

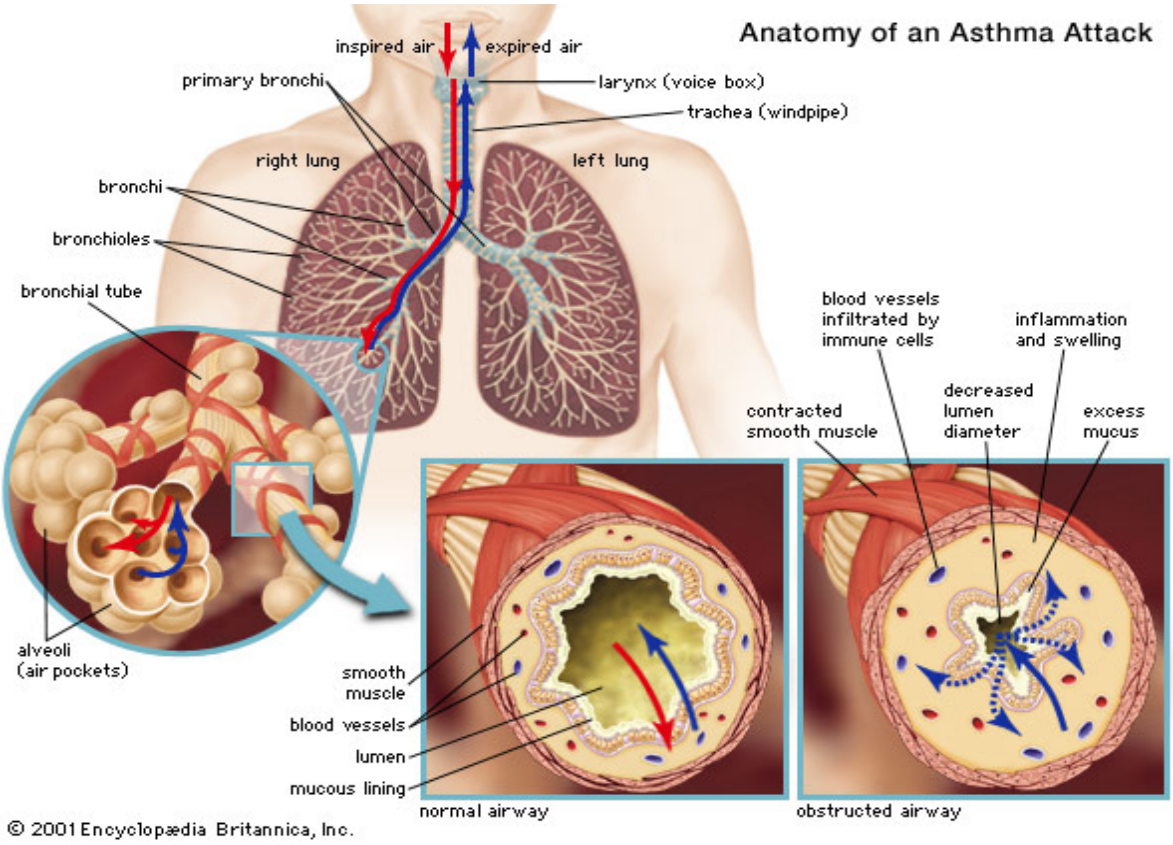
Definition

The Global Initiative for Asthma (GINA) defines asthma as a chronic inflammatory disease of the airways in which many cells and cellular elements play a role. The chronic airway inflammation is associated with airway hyper responsiveness (AHR) that leads to recurrent episodes of **wheezing, shortness of breath, chest tightness and coughing** particularly at night or in the early morning. These episodes are usually associated with widespread but variable airways obstruction within the lung that is often reversible either spontaneously or with treatment.

The key components of this definition include:

- The presence of airway inflammation
- Airway hyper responsiveness which implies that the airways will narrow easily and too much in response to various stimuli
- Recurrent episodes of symptoms of wheezing, breathlessness, chest tightness and coughing
- Reversible airways obstruction that is demonstrable by changes in lung function (Forced Expiratory Volume in 1 second and Peak Expiratory Flow) in response to a broncho-dilating agent such as salbutamol.

Figure 13.1 Summary of Airway Pathophysiologic Process in Asthma



Burden

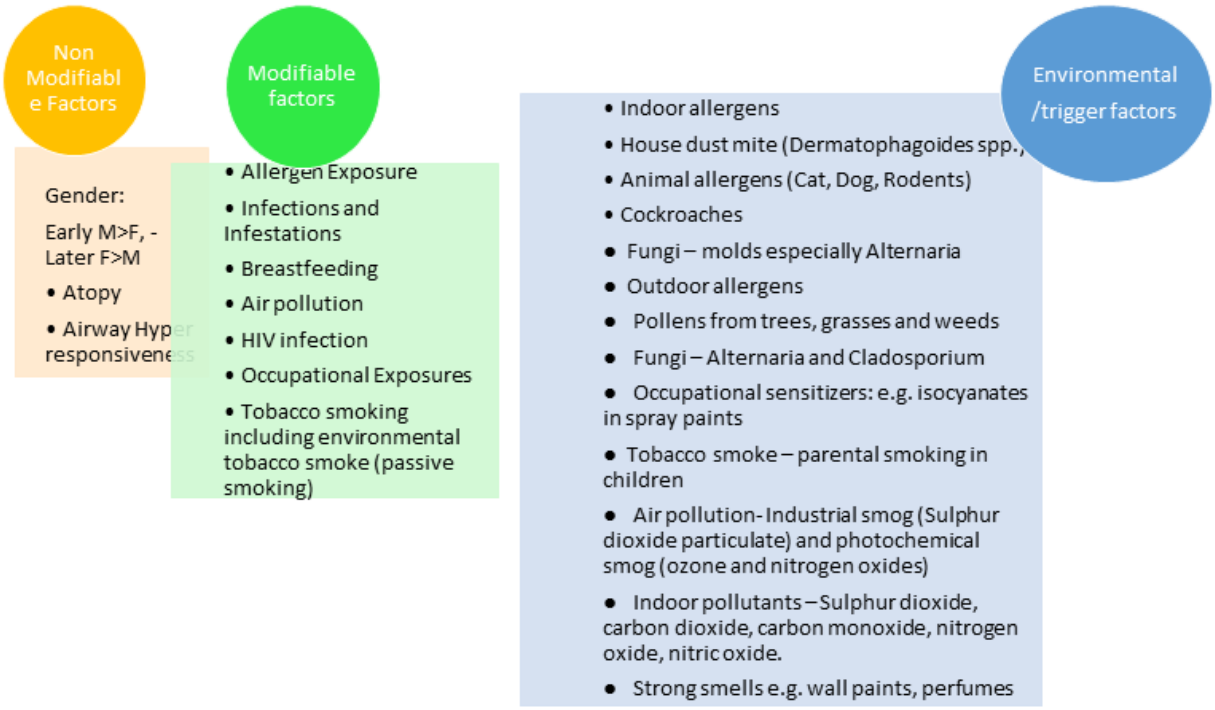
Globally an estimated 339 million people suffer from asthma with an associated mortality of 383,000 annually. From the International Study of Asthma and Allergic Disease in Childhood (ISAAC), Kenya has an estimated prevalence of 10% of the population with asthma, approximately 4 million people. The prevalence of wheeze in the past 12 months among 13- 14 year olds was 18% and 13.8 % in Nairobi and Eldoret respectively in the year 2000 up from17.1% and 10.4 % in 1995. The prevalence of asthma in older children between the ages of 12-14 years may be increasing.

Risk factors

Asthma is a heterogeneous disease and there are several phenotypes based on

- Whether allergic or not
- Control (poor control, controlled and brittle)
- Time of onset (childhood or late in adulthood)
- Occupational
- Trigger(s)

Figure 13.2: Risk factors for Asthma



Clinical Presentation of asthma

A history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, and variable expiratory airflow limitation. This is most likely asthma but Lung function test (spirometry) where available should be done.

Table 13.2 Typical and atypical presentation of asthma

Typical presentation	Atypical presentation
• Frequent episodes of cough, chest tightness, breathlessness and wheezing that vary in duration and severity • Symptoms occur mainly at night and wake up patient, usually in the early hours of the morning • Symptoms 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 remodeling • 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

Diagnosis of 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?
- Is there a family history of allergy/atopy i.e allergic conjunctivitis, allergic rhinitis, asthma, eczema and food (protein) allergy?

Obtain a Lung Function Test to assess airway hyper-responsiveness (measure FVC, FEV_1 and PEF) by Spirometry, where available. Peak expiratory flow meter (PEFM) is cheaper and should be used where there's no spirometer.

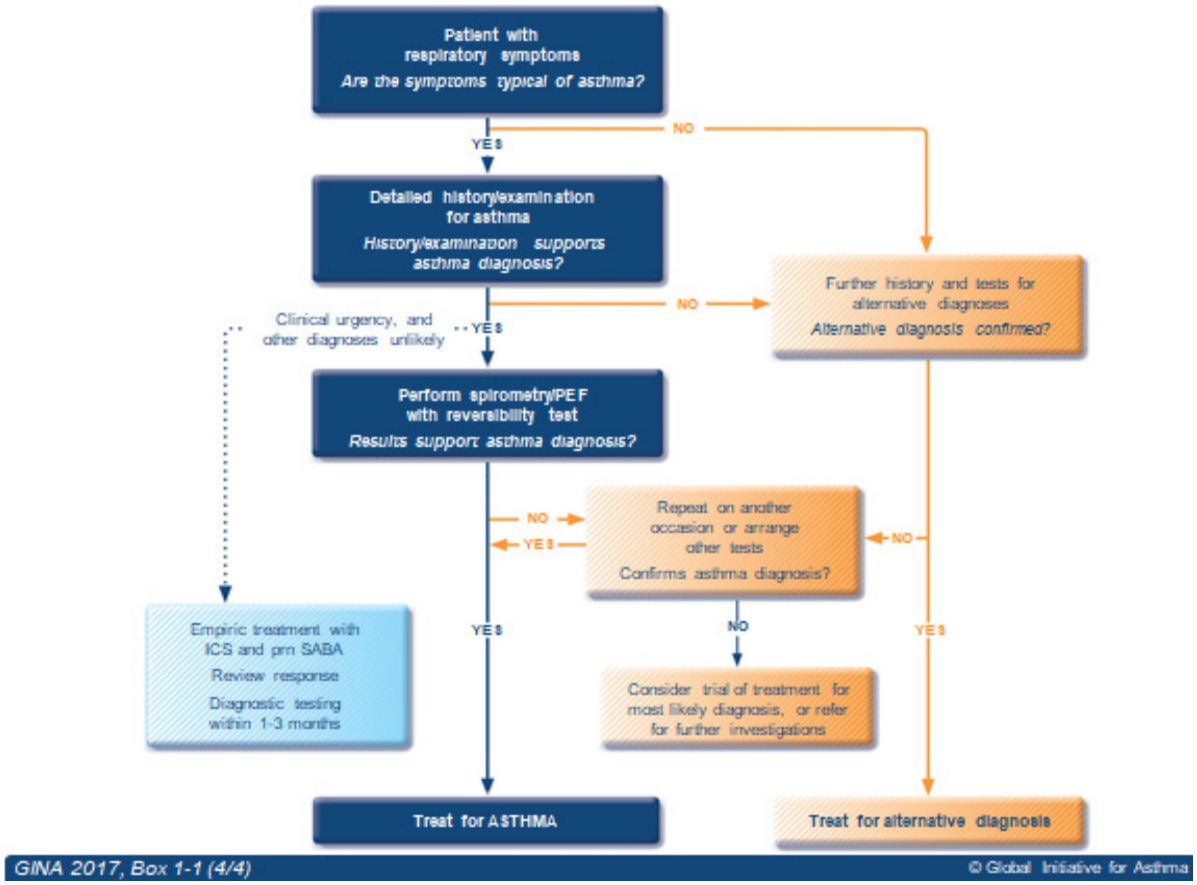
- Is there airflow limitation (FEV_1/FVC less than 85 or diurnal variation in PEF)? FEV_1/FVC < 85% in children and 75% in adults is indicative of obstructive airway disease.
- Is there a bronchodilator response (FEV_1 or PEF improvement by greater than 12.5% (or 200mls), or 20% respectably, 30 minutes 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)
- Does the FEV_1 drop below 20% with only small doses of inhaled bronchoconstrictors such as Methacholine, Histamine or with exercise?

Diagnosis of asthma in children

The general principles for the diagnosis of asthma apply to children. Many preschool children have frequent wheezing and most (over 50%) of those treated as asthma will not have typical symptoms later on in life. Children with recurrent wheeze should be given a trial of anti-asthmatic medication. Children with the following features are most likely to be asthmatic:

- Frequent episodes of chronic cough, chest tightness, breathlessness and wheeze particularly experienced at night, early morning, or in response to exercise, common allergens, emotions, laughter or occur in the absence of 'common cold' if they respond to asthma treatment.
- Wheeze in between viral infection
- A strong family history of asthma or allergic disease is also supportive of the diagnosis of asthma in very young children.

Figure 13.3: Diagnostic flow-chart for asthma in clinical practice



Classification of asthma

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

Table 13.3: 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%

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

Table 13.4: Asthma Medications are classified into two broad groups:

Relievers	They reverse broncho-constriction and relieve its symptoms. They include rapid and short acting, rapid and long acting bronchodilators. Short acting bronchodilators: Salbutamol
Controllers	They are taken daily to keep asthma under control through their anti – inflammatory effects
	Long Acting $_2$ Agonists (LABA) have anti-inflammatory effects, 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. Beclomethasone Dipropionate Budesonide Ciclesonide Fluticasone Propionate

Management of acute asthma

Acute asthma is classified as:

- Mild asthma attack,
- Moderate asthma attack and
- Severe asthma attack.

Management of severe asthma

- Symptoms of severe asthma Identification: Talks in words, Sits hunched forward, Agitated,Respiratory rate >30 p/m,Accessory muscles in use,Pulse rate>120bpm, O_2 Saturation (on air) < 90% , PEF≤50% predicted or best
- **Life threatening asthma:** Drowsy,confused, silent chest
- Treat as urgent
- Transfer to acute care facility
- While waiting for transfer to acute care facility: give SABA by nebulizer, O_2, systemic corticosteroid, immediately give inhaled SABA, inhaled ipratropium bromide
- In acute care facilities intravenous magnesium sulfate may be considered if the patient is not responding to intensive initial treatment.

FOLLOW UP

Management of Mild to Moderate

- ***Mild or Moderate asthma****-Talks in phrases, Prefers sitting to lying,Not agitated, Respiratory rate increased, Accessory muscles not used, Pulse rate 100-120bpm, Oxygen saturation on air 90-95%, PEF >50% predicted or best*
- 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

Treatment

- SABA 4-10Puffs pMDI + Spacer, repeat every 20mins for 1 hour
- Use prednisolone: adults-1mg/kg max.50mgs. Children:1-2mg/kg max.40mg
- Control oxygen (if available), target saturation 93-95% (children 94-98%)
- Assess response at 1 hour, if improving assess for discharge (symptoms improved, not needing SABA, PEF improving, and >60-80% of personal best or predicted, oxygen saturation >94%)

Discharge treatement

- Reliever: as needed rather than routinely
- Controller: stat or step up, check inhaler technique and adherence
- Prednisolone: continue for 5-7days (3-5days) for children
- Follow up within 2-7 days

Follow up

- Reliever: as needed rather than routinely
- Controller: continue higher dose for short term (1-2 weeks) or long term (3 months), depending on background to exacerbation.
- Risk factors: check and correct modifiable risk factors that may have contributed to the exacerbation, including inhaler technique and adherence.
- Action Plan: is it understood? Was it used appropriately? Does it need modification?
- **IF WORSENING CONDITION (manage as severe acute asthma):**
  - Transfer to acute care facility
  - While waiting give SABA, O_2, systemic corticosteroid
- NB: PEF-Peak expiratory flow; SABA-short acting beta$_2$- agonists (doses are for salbutamol)

Management of chronic asthma

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
4. Regular assessment of patients for their symptom control.

Table 13.5: Assessment of asthma symptom control

In the past 4 weeks, has the patient had;	Yes	No
Daytime symptoms of asthma (cough, wheeze, shortness of breath more than twice/week etc)?		
Any night waking due to asthma?		
Reliever needed more than twice/week?		
Any activity limitation due to asthma?		
Score: Well controlled - None of these, Partially controlled - 1-2 of these, Uncontrolled - 3-4 of these		

Medication for chronic care

Long Acting $_2$ Agonists (LABA) have anti-inflammatory effects and are used in combination with inhaled corticosteroids (ICS) for the long-term control of asthma. They also inhibit mast cell mediator release, plasma exudation and reduce sensory nerve activation. Anti-inflammatory therapy (ICS) forms the backbone of asthma control.

All asthma patients should be on inhaled corticosteroids. Bronchodilators should not be used without combining with ICS, since asthma is an inflammatory disease. Frequent use of SABA can lead to excess deaths due to side effects and failure to address the inflammatory aspect.

Inhaler Devices

- Pressurized Metered Dose Inhalers (pMDIs)
- Breath Actuated MDIs
- Dry Powder Inhalers
- Soft Mist Inhalers
- Nebulizers or wet aerosols
- Volume Spacers with or without face masks to be used with pMDIs

Management of poor responders

- The first step is to exclude alternative diagnose
- The second is to consider and exclude comorbidities
- The third Assess adherence to medication
- The fourth step involves identifying the pattern of inflammation and response to treatment. Innovative biological therapies can be used.

Table 13.6: Other medications used in asthma management

Anticholinergics	They are used for the treatment, especially in the acute care setting. Ipratropium bromide is usually combined with a short acting B_2 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

Table 13.7: Differential diagnosis of asthma

Non asthma causes of cough and or wheeze in children	**Non asthma causes of cough and or wheeze in adults**
• Chronic rhino- sinusitis • Recurrent viral respiratory tract infections • Foreign body aspiration • Gastro –esophageal reflux • Tuberculosis • Congenital heart disease • Cystic fibrosis • Bronchopulmonary dysplasia • Congenital malformations with narrowing of the airways • Primary ciliary dyskinesia syndrome • Immune deficiency • Bronchiectasis	• Tuberculosis • Chronic bronchitis and COPD • Bronchiectasis • Heart disease • Airway obstruction e.g. lung cancer, tracheal stenosis etc

Table 13.8: Approaches To Identifying Asthma Differentials

Diagnosis	Evaluation
Upper Airway Disease • Adeno-tonsillar hypertrophy • Rhino-sinusitis • Post Nasal Drip	• Clinical ENT Examination • Sinus X-ray • CT Paranasal Sinuses • ENT Specialist Referral

Diagnosis	Evaluation
Congenital Structural Bronchial Disease • Tracheo- bronchomalacia • Cartilage Rings • Cysts • Webs	• Bronchoscopy • CT Scan Chest
Bronchial/ Tracheal Obstruction • Vascular Rings/ Slings • Enlarged Cardiac Chamber • Lymph Node Enlargement from TB or Lymphoma	• CXR • CT Scan Chest • Echocardiogram • Mediastinoscopy
Endobronchial Disease Foreign Body /Tumor	• Chest X-ray • Bronchoscopy
Esophageal / Swallowing Problems • Reflux • Uncoordinated Swallowing • Laryngeal Cleft • Tracheo-esophageal Fistula	• Upper GI Studies/Barium Swallow • Upper Endoscopy • PH Probe • Milk Scan
Pulmonary Suppuration • Cystic Fibrosis • Primary Ciliary Dyskinesia • Severe Immunodeficiency Syndromes • Agammaglobulinemia	• Sweat/Genetic testing • Lung/Sinus Biopsy/Molecular Genetic Testing • Complete Blood Count • Immunoglobulin Levels • Complement Levels
Miscellaneous • Post Viral Wheeze • Acute Bronchiolitis. • Laryngo-Tracheobronchitis	• Characteristic Viral Syndrome • Antigen Tests for RSV • Viral Cultures • PCR • CXR
Chronic obstructive pulmonary disease	• Spirometry
Congestive heart failure	• Echocardiogram • Serum BNP
Pulmonary embolism	• Chest X-ray • Lower limb doppler ultrasound • CT pulmonary angiogram • Echocardiogram • Perfusion/ventilation scans
Tumors	• Contrast enhanced CT scan chest
Pulmonary eosinophilia	• Sputum eosinophilia • Elevated eosinophil counts in full haemogram.

Diagnosis	Evaluation
ACE Inhibitor induced cough	Medication review and discontinuation of ACE inhibitors
Vocal cord dysfunction	Bronchoscopy
Laryngeal dysfunction	Laryngoscopy

13.2 Chronic 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.

RISK FACTORS

- Age and Sex: Elderly >40 years and Female > Male
- Environmental factors:
  - Active tobacco smoking
  - Secondary tobacco smoking
  - Indoor air pollution - bio fuels and coal

  Outdoor air pollution-also contributors to the lungs' total burden of inhaled particles
- Occupation exposure:
  - Organic and inorganic dust
  - Chemical agents and fumes
- Genetic factors-
  - Severe hereditary deficiency of alpha-1 antitrypsin (AATD), the gene encoding matrix metalloproteinase-12 (MMP-12) and glutathione S-transferase have also been related to decline in lung function or risk of COPD
- Lung growth and development – any factor that affects lung growth during gestation and childhood (low birth weight, respiratory infections, etc.) has the potential to increase an individual's risk of developing COPD
- Socio-economic status -poverty is consistently associated with airflow obstruction and lower socio-economic status is associated with an increased risk of developing COPD.
- Asthma and airway hyper-reactivity - asthma may be a risk factor for the development of airflow limitation and COPD
- Infections-
  - History of severe childhood respiratory infection has been associated with reduced lung function and increased respiratory symptoms in adulthood
  - Post Tuberculosis lung damage
  - Chronic bronchitis - may increase the frequency of total and severe exacerbations

Diagnosis of COPD

Consider COPD in a patient with:

- Dyspnea that is progressive, persistent and worsens with exercise
- Chronic cough which may be intermittent and productive or not productive
- 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

- Spirometry is the Gold standard for clinical diagnosis and monitoring COPD
- Post bronchodilator FEV1/FVC less than 70% confirms the presence of persistent airflowlimitation
- To diagnose, manage and follow up COPD patients one should have access to Spirometryfacilities

Distinguishing asthma and COPD: a 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

Table 13.9: If the cause of wheezing is not known, distinguish COPD and asthma as follows

ASTHMA	**COPD**
• 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/or had TB • Previous diagnosis of COPD **COPD likely** • Confirm diagnosis - Give routine COPD care

Table 13.10 Other Differentials of COPD

Diagnosis	Suggestive features
Congestive heart failure	Chest X-ray shows a dilated heart, pulmonary edema Pulmonary function test indicate volume restriction, not airflow limitation.
Bronchiectasis	Large volume of purulent sputum Commonly associated with bacterial infection Chest X-ray/CT scan shows bronchial dilatation, bronchial wall thickening
Tuberculosis	Onset all ages Chest X-ray shows lung infiltrates Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiolitis	Onset at a younger age, non-smokers May have a history of rheumatoid arthritis or acute fume exposure Seen after lung or bone marrow transplantation CT on expiration shows hypodense areas
Diffuse panbronchiolitis	Predominantly seen in patients of Asian descent Most patients are male and non-smokers Chest X-ray and HRCT show diffuse small centrilobular nodular opacities and hyperinflation

Management of COPD

Goals of COPD management

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

Assess COPD severity and the extent 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).

Table 13.11 Classification of severity of COPD based on Post bronchodilator FEV_1 (in patients with FEV_1/FVC <0.70)

GOLD 1	Mild COPD	FEV_1 ≥ 80% predicted
GOLD 2	Moderate COPD	50% ≤ FEV_1 <79% predicted
GOLD 3	Severe COPD	30% ≤ FEV_1 < 49% predicted
GOLD 4	Very Severe COPD	FEV_1 < 30% predicted

Assess risk for exacerbations

Exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond 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 includes:

1. Smoking cessation: This 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.
   c) Institution of smoking prevention and tobacco control strategies (*Refer to National Tobacco Control policies*)

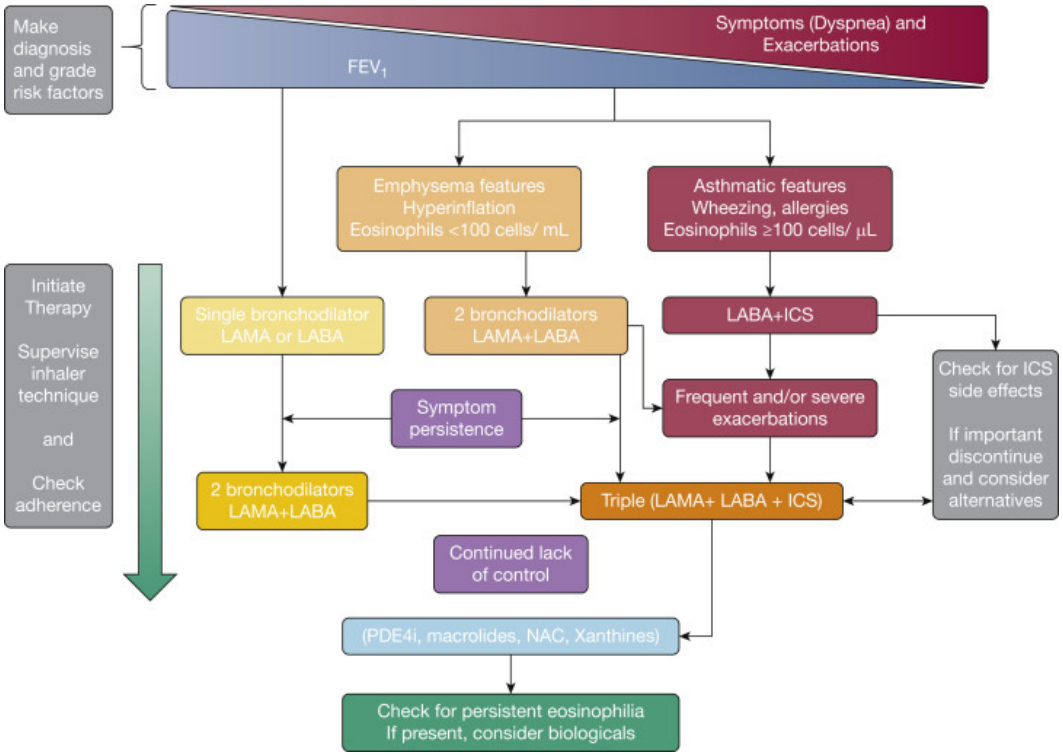
2. Prevention of occupational exposure

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:
   i. Inhaled bronchodilators
   ii. Inhaled corticosteroids
   iii. Combined inhaled corticosteroid/ bronchodilator therapy is more effective than individual components. Antibiotics are not recommended except for treatment of suspected bacterial infections.
   iv. Mucolytic agents for patients with viscous sputum
   v. Oxygen therapy - Long term administration of oxygen for > 15 hours per day has been shown to increase survival in patients with severe COPD
   vi. 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 comorbidities e.g. cardiovascular diseases, malignancies and progressive respiratory failure

Figure 13.4 Guide for the management of COPD based on severity of the disease



Key: *LAMA - Long Acting Muscarinic Antagonist, LABA - Long Acting Beta Antagonist, ICS - Inhaled Corticosteroids, PDE4i-Phosphodiesterase 4 inhibitors, NAC - N-Acetylcysteine*

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.

Treatment of acute exacerbations

Lower respiratory tract infections (LRTI) 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.

13.3 Post-Tuberculosis Lung Disease (PTLD)

The World Health Organization (WHO) estimates that 1.7 billion people are infected with *M. tuberculosis* globally and approximately 54 million people survived Tuberculosis (TB) between 2000 and 2017 alone. Kenya for instance notified 96,478 patients with TB in 2018 and successfully treated 84% of them. There is increasing evidence of long-term respiratory complications following TB in a proportion of these patients affecting their quality of life. For many persons with tuberculosis, a microbiological cure is the beginning, not the end of their illness.

Post TB Lung Disease (PTLD) is defined as chronic respiratory abnormality with or without symptoms attributable, at least in part, to previous pulmonary TB.

There is evidence that over 60% of patients still have symptoms after completion of TB treatment, over 80% have radiological sequalae, over 30% have spirometric function test abnormalities and over 40% have bronchiectasis *(Meghji J, et al 2020 [https://thorax.bmj.com/content/75/3/269]).*

Patients with PTLD may present with persistence of symptoms or decline in lung function despite successful completion of treatment or cure.

Patients presenting with respiratory complaints and have recently completed TB treatment (and who may be erroneously considered as TB relapse) should be thoroughly evaluated for post-TB lung disease and/ or other forms of lung conditions.

Post TB lung disease may present as the following:

1. Lung scarring (fibrosis)
2. Bronchiectasis
3. Chronic Obstructive Pulmonary Disease (COPD)
4. Lung abscess
5. Aspergillus-related lung disease
6. Spontaneous Pneumothorax

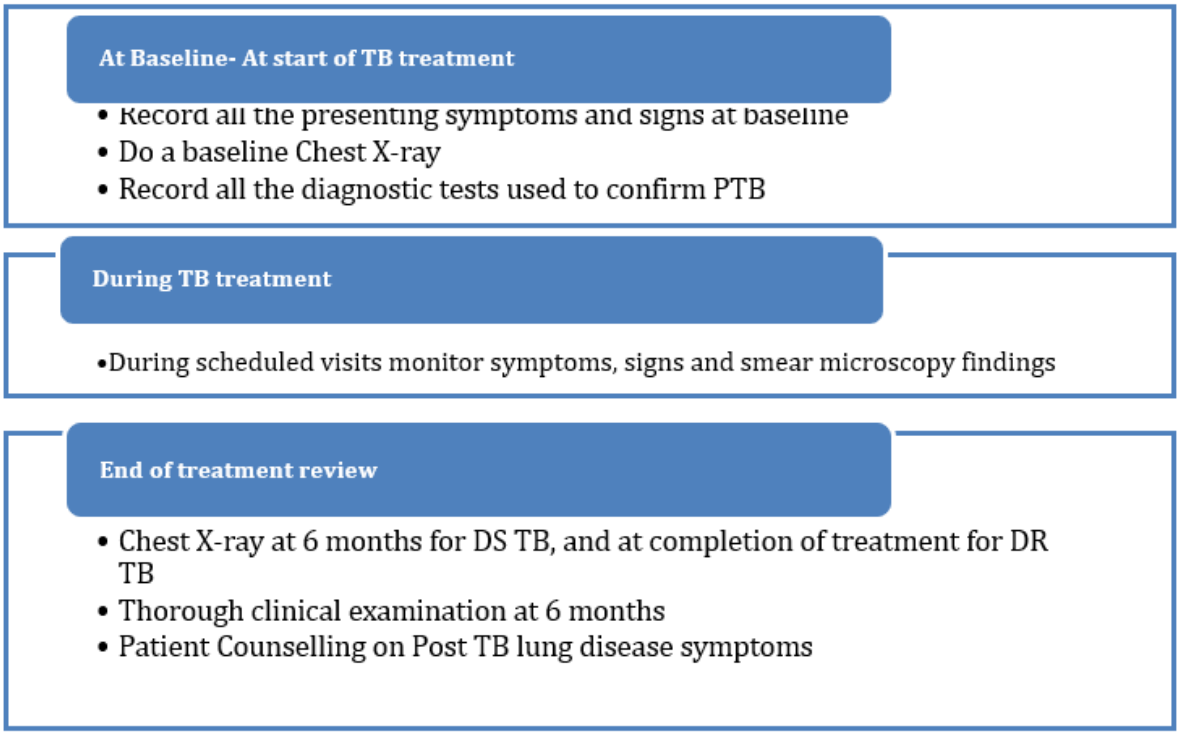
Clinical Presentation of PTLD

This is dependent on the type of lung impairment and presentation is varied. The key presentation of PTLD is persistence of clinical symptoms or occurrence of new symptoms e.g. cough, chest pains, breathlessness or decline in lung function despite successful completion of PTB treatment.

Assessment for Post TB Lung Disease

Assessment of post TB Lung disease should begin with a baseline assessment at the initiation of PTB treatment followed by regular assessment during and after successful completion of PTB treatment.

Schedule of assessment:



Possible outcomes at end of treatment review

A. Patients with normal CXR and no symptoms-**Discharge** from clinic and advise to come back if the develop any symptoms

B. For patients with symptoms but normal CXR-

Do spirometry and manage as appropriate (Eg COPD management), If symptoms persist refer

C. Patients with abnormal CXR but no symptoms- If minor findings eg calcification, fibrosis, pleural thickening- schedule follow up after 6 months

If major findings eg pleural effusion, pneumothorax, lung mass, cardiac abnormalities- **Refer to physician/surgeon** as appropriate for management-High Resolution CT scan is required

D. For patients with symptoms and abnormal CXR-

Investigate- Full blood count, sputum culture,

Do spirometry

Manage as appropriate and refer to physician if symptoms persist

Review at Month 12, 18 and 24 after the end of treatment

- All B,C,D patient categories above should be reviewed at 12, 18 and 24 months.

- History: Symptom enquiry form
  - Cough
  - Hemoptysis
  - Sputum
  - Chest pain
  - Breathlessness
- Clinical examination
  - Vital signs- Respiratory rate, Heart rate
- Nutritional status- BMI
- Full physical examination

Other radiological investigations as indicated:

Lung parenchyma diseases (Interstitial diseases) - High Resolution CT Scan

Cardiac involvement - Cardiac CT scan

Mediastinum, chest wall involvement - Chest CT Scan

Table 13.12 Diagnosis - Possible Post TB Lung Disease clinical pattern

Compartment	Clinical Pattern	Definitions
Airways	Tuberculosis associated obstructive lung disease	Airway obstruction (FEV_1/FVC ratio < 0.7 or <LLN) though primarily related small airway disease
	Bronchiectasis	CT definition - evidence of airway dilatation; more than diameter of adjacent vessel, or non-tapering. OR CXR definition-evidence of ring and tramlines
Parenchyma	Cavitations	A gas-filled space either within an area of pulmonary consolidations, or surrounded by a thin wall
	Parenchymal destruction	Extensive destruction of lung tissue, with a gas-filled space occupying the volume of ≥1 lobe
	Fibrotic change	Areas of parenchymal scarring, with associated volume loss
	Aspergillus related lung disease	Evidence of aspergilloma on imaging or chronic pulmonary aspergillosis on imaging and blood testing
Pleural	Chronic pleural disease Evidence of pleural thickening on CXR or CT imaging	
Pulmonary vasculature	Pulmonary hypertension	Elevated pulmonary arterial pressures as estimated using doppler echocardiography or measured at right heart catheterization
Other	Other	Other pathology not meeting the criteria above.

Adapted from the 1st symposium on post TB lung disease on July 2019

Management of Post TB Lung Disease conditions:

The management is dependent on the diagnosis.

1. Lung scarring (fibrosis)

Definition - Thickening, scarring or stiffness of lung tissue making it less efficient in the ability to get oxygen into the bloodstream. There is normally associated volume loss. Develops as a consequence of lung healing, e.g. from TB.

The stiffness causes difficulty in lung expansion leading to shortness of breath. This could be a sequelae of extensive tuberculous disease.

Clinical presentation:

Symptoms- The symptoms depend on the extent of fibrosis. Patients may be asymptomatic or experience dry cough. In severe cases- shortness of breath on exertion, decreased exercise tolerance, finger clubbing

Clinical examination

Diagnosis:

Radiological appearance

Commonly occurs at the apices and upper lobes, with fibronodular opacities and associated loss of lung volume. Elevation of the adjoining fissure or hilum may be associated.

Scaring appearing beyond 6 months can help distinguish active TB from healed TB.

Management:

- There is no cure and management is to relieve symptoms and reduce further lung scarring.
- In severe terminal cases, long-term oxygen therapy may be required.
- These patients should be referred for review and specialised care by a physician.

2. Bronchiectasis

Definition: This is a chronic lung disease often secondary to an infectious process that results in the abnormal and permanent distortion and widening of airways leading to build-up of excess mucus. Mechanisms for pathogenesis of bronchiectasis are infection, airway obstruction and peribronchial fibrosis.

Clinical presentation:

Symptoms:

- Cough and daily mucopurulent sputum production, often lasting months to years (classic)
- Blood-streaked sputum or hemoptysis from airway damage associated with acute infection
- Dyspnea, pleuritic chest pain, wheezing, fever, weakness, fatigue, and weight loss
- Rarely, episodic hemoptysis with little to no sputum production (i.e., dry bronchiectasis)

Clinical examination

Diagnosis:

The diagnosis of bronchiectasis involves the following:

- A compatible history of chronic respiratory symptoms (e.g., daily cough and purulent sputum production)
- Tests recommended for aetiological testing in adults:
    1) Differential blood count
    2) Serum immunoglobulins (total IgG, IgA and IgM)

3) Testing for allergic bronchopulmonary aspergillosis (ABPA)

4) Sputum culture for bacterial infection

5) Mycobacterial culture for NTM

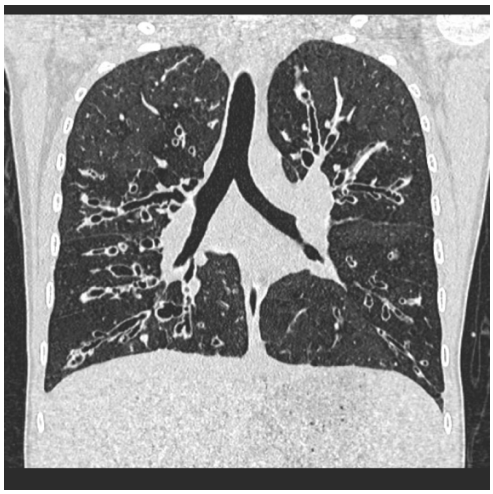
Additional tests may be appropriate in response to specific clinical features, or in patients with severe or rapidly progressive disease.

Radiological appearance:

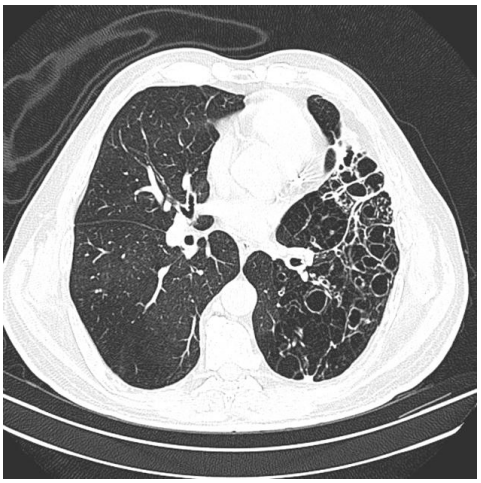
Imaging plays a pivotal role in the diagnosis of bronchiectasis.

High-resolution computed tomography (HRCT) is the cornerstone in the radiological diagnosis of clinically suspicious cases and the most sensitive and specific non-invasive method for diagnosing bronchiectasis. Additionally, the pattern of disease on HRCT may enable one to limit the differential to a single/few specific causative entities.

Figure 13.5: HRCT Chest (a) axial and (b) coronal images showing cystic and varicose bronchiectatic changes with retraction due to fibrosis



(a) HRCT axial chest



(b) HRCT Coronal Chest

The CXR: This has a role largely in surveillance for intercurrent infection, progressive lobar collapse or suspected development of cavitary disease in patients with known bronchiectasis.

The affected individuals are often normal or show nonspecific findings. The key changes to look for include parallel line opacities (tramtrack appearance), tubular opacities (mucus plugging) and ring opacities (dilated end on bronchi). others are Lobar atelectasis and compensatory hyperinflation.

Management

Treatment is mainly aimed at reducing exacerbations. These are associated with increased airways, systemic inflammation and progressive lung damage.

In addition, more severe and more frequent exacerbations are associated with worse quality of life, daily symptoms, lung function decline, and mortality.

The cycle below shows the different cycles that a patient goes through.

Figure 13.6: Treatments for bronchiectasis according to the vicious cycle concept of bronchiectasis

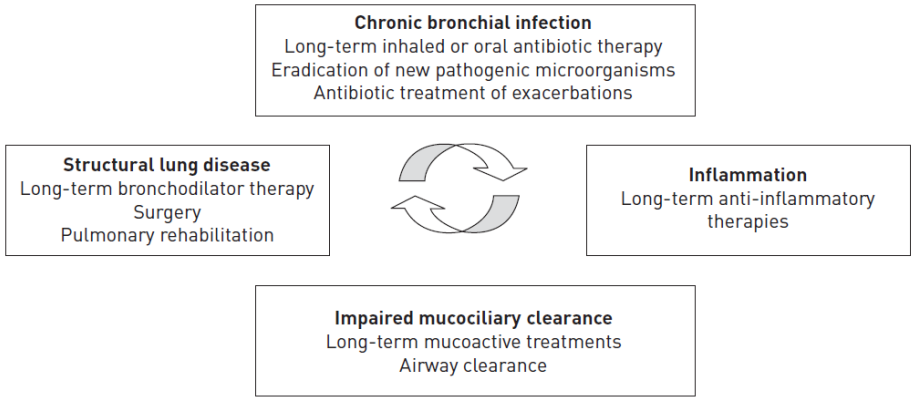


FIGURE 1 Treatments for bronchiectasis considered in this guideline according to the vicious cycle concept of bronchiectasis.

- Chest physiotherapist: This includes postural drainage and other maneuvers aimed at improving drainage of respiratory secretions.
- Antibiotics: Infective exacerbations will require antibiotics. Broad-spectrum antibiotics like amoxicillin-clavulanate, metronidazole or clindamycin for anaerobic infection.

  Antipseudomonal antibiotic like ciprofloxacin, 3rd generation cephalosporin (e.g., ceftazidime) should be used when colonization with Pseudomonas is suspected.
- If haemoptysis is severe and life threatening, patients should be admitted to hospital

  for more specialized treatment

NB: *Once a diagnosis is made, REFER to a chest physician for further specialized care*

3. Chronic Obstructive Pulmonary Disease (COPD)

Definition: COPD 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.

TB disease can result into a COPD-like airway disease, at times called TB-associated COPD.

Clinical Presentation:

Usually it presents with cough, difficulty in breathing, tight chest and wheezing. A substantial number of TB patients develop post-tubercular airway disease or TB-associated 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
- 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

Diagnosis:

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.

Management:

For detailed management refer to COPD section

4. Lung abscess

Definition: A lung abscess is a bacterial infection that occurs in the lung tissue. The infection causes tissue death, and pus collects in that space. A lung abscess can be challenging to treat, and it can be life threatening. Often seen in a patient with extensive damage to the lungs after tuberculosis.

Clinical presentation:

Symptoms: The most noticeable symptom of a lung abscess is a productive cough. The contents that are coughed up may be bloody or pus-like, with a foul odour, fever of 38 degrees celsius or higher, chest pain, shortness of breath, sweating or night sweats, weight loss, fatigue.

Clinical examination

Dullness on percussion and decreased or absent breath sounds with an intermittent pleural friction rub (grating or rubbing sound) on auscultation, crackles may present.

Diagnosis:

Rule out TB and other infections by conducting sputum or pus analysis, CXR and/or CT. Full blood count and/or a blood culture will support establishing the causative agent.

Management of abscess

- 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.

NB: *Once a diagnosis is made, REFER to a chest physician for further specialized care*

5. Aspergillus-related lung disease

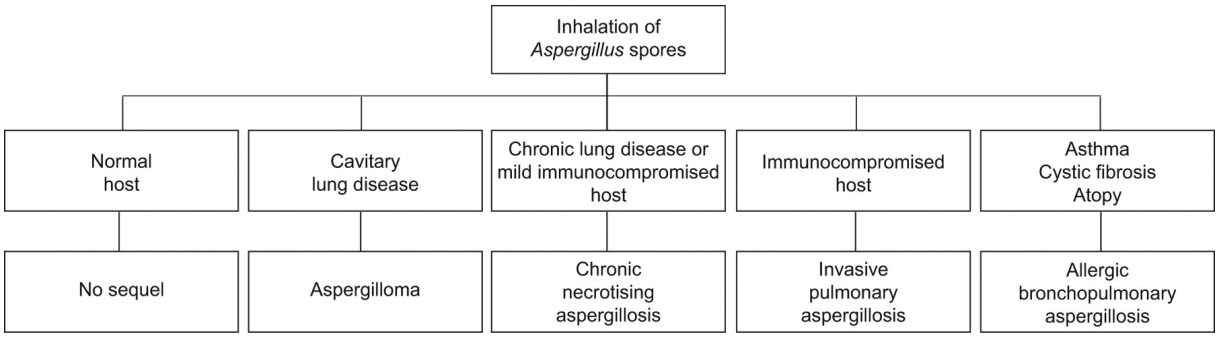
Definition: This results from colonization of tuberculous cavities or bronchiectatic lesions with the fungus Aspergillus.

Three distinctive patterns of aspergillus-related lung disease are recognized:

- Saprophytic infestation of airways, cavities and necrotic tissue
- Allergic disease including extrinsic allergic alveolitis, asthma, allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis and
- Chronic eosinophilic pneumonia.

They manifest depending on the underlying lung pathology and host immune status into the following 5 types.

Figure 13.7: Classification of Aspergillosis



Clinical presentation:

Signs and Symptoms: These vary depending on the severity and type of illness one develops. Three distinct types are known with specific signs and symptoms.

Table 13.13: Signs and Symptoms of Aspergillosis

Type of illness	Signs / symptoms	Predisposing condition
Allergic reaction *(allergic bronchopulmonary aspergillosis)*	• *Fever* • *A cough that may bring up blood or plugs of mucus* • *Worsening asthma*	*Develops in asthma or cystic fibrosis*
Aspergilloma	• *Normal initially* • *A cough that often brings up blood (haemoptysis)* • *Wheezing* • *Shortness of breath* • *Unintentional weight loss* • *Fatigue*	*Emphysema, tuberculosis or advanced sarcoidosis,*
Invasive aspergillosis *(Most severe form and fatal)*	*Signs and symptoms depend on which organs are affected, Generally:* • *Fever and chills* • *A cough that brings up blood (haemoptysis)* • *Shortness of breath* • *Chest or joint pain* • *Headaches or eye symptoms* • *Skin lesions*	*In people whose immune systems are weakened as a result of cancer chemotherapy, bone marrow transplantation or a disease of the immune system to the brain, heart, kidneys or skin*

Table 13.14 Diagnosis of Aspergillosis

Diagnostic spectrum		
Allergic bronchopulmonary aspergillosis (**ABPA)**	**Invasive aspergillosis (Chronic necrotizing Aspergillus pneumonia)**	**Aspergilloma**
Laboratory testing		
Major: Blood: *CBC for Eosinophilia.* *-Skin test - positive result for A. fumigatus* *-Marked elevation of the serum immunoglobulin E (IgE) level to greater than 1000 IU/dL* *- Aspergillus Precipitin test: positive results for Aspergillus precipitins (primarily immunoglobulin G [IgG], but also immunoglobulin A [IgA] and immunoglobulin M [IgM])*	Demonstration of the organism in sputum	

-***Minor criteria*** *- positive Aspergillus radioallergosorbent assay test results* *Sputum culture for Aspergillus in sputum and* *Culture / sensitivity*		
Imaging		
Chest radiography *-Fleeting pulmonary infiltrates* *- Mucoid impaction* *-central bronchiectasis* *- Lobulated infiltrate, which has been likened to a cluster of grapes or a hand in a mitten* ***HRCT*** *Mucus filled bronchi* *Areas of atelectasis*	***Chest radiography*** ***-****Variable features with variable, solitary or multiple nodules* *- Cavitary lesions* *- Alveolar infiltrates that are localized or bilateral* *- Diffuse infiltrates as disease progresses* ***HRCT*** *-Characteristic halo sign (i.e., an area of ground-glass infiltrate surrounding nodular densities)* *-Later disease may show a crescent of air surrounding nodules, indicative of cavitation.* *-Because Aspergillus is angioinvasive, infiltrates may be wedge-shaped,* *-Pleural-based, and cavitary, which is consistent with pulmonary infarction*	***Chest radiography*** *-A mass in a preexisting cavity,* *-Usually in an upper lobe* *- manifested by a crescent of air partially outlining a solid mass.* *- Movement of mass with position* ***HRCT*** *- Better definition of the mass within a cavity* *- May demonstrate multiple aspergillomas in areas of extensive cavitary disease (supine and prone CTs to be considered)*

- High levels of specific immunoglobulin G against Aspergillus in blood (Confirmatory test)

Management

- The only effective treatment is surgical removal of the aspergilloma. In addition to surgical removal: Oral itraconazole may provide partial or complete resolution of aspergillomas in 60% of patients.
- Antifungal medicine can be used for invasive pulmonary aspergillosis e.g., Amphotericin B and voriconazole.

6. Spontaneous Pneumothorax

Definition: It is the presence of air in the pleural cavity resulting in 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.

Clinical presentation:

Symptoms:

- Acute onset shortness of breath
- Chest pain.

Diagnosis:

Pneumothorax is generally diagnosed using a chest X-ray. In some cases, a computerized tomography (CT) scan may be needed to provide more-detailed images

Management:

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

NB: Once a diagnosis is made, REFER to a chest physician for further specialized care

13.4 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 lung tissue elasticity. The lung loses its ability to supply oxygen to the bloodstream and as the scarring progresses, one loses the ability to breath. ILDs can coexist with other lung diseases.

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 acutely.

Causes of ILDs

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

For those with known causes, some known causes include:

- 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
- 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 Erythematosus (SLE). Chest symptoms may be the first signs/symptoms of these autoimmune diseases long before other organ symptom manifestations.
- 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
- Sarcoidosis
- Genetics

Some of the common ILDs include:

1. Those of known causes;
    a. Pneumoconiosis (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. They vary from moderate to severe and may include the following;

- 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 'velcro' crackles of the lung bases on auscultation due to fibrosis.

Diagnostic test

- Chest X Ray and Chest CT scan which show signs of scarring/fibrosis, interstitial lung markings, loss of lung volume.
- Lung function tests- Spirometry to assess for lung restriction.
- Blood test depending on suspected cause. e.g. autoimmune antibodies screen for connective tissue disease.
- Lung biopsy – bronchoscopy.

Management of ILDs

Corticosteroids such as prednisone are be used with supportive oxygen therapy and pulmonary rehabilitation

13.5 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.

Predisposing factors include:

- Smoking - both active and passive is responsible for up to 80 – 90% of cases
- Asbestos exposure
- Family history of lung cancer
- Chronic lung diseases
- Prior history of lung cancer

Diagnosis

Clinical presentation

Lung cancer does not usually cause symptoms in its early stages. Most patients will present with clinical signs on first visit, but a minority (20%) may be diagnosed incidentally.

Symptoms may be directly related to local effects (tumour itself or pressure effects) of the cancer or to endocrine or metastatic effects.

Clinical symptoms of lung cancer

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

Radiology diagnosis

a) Chest radiography - This is the initial imaging evaluation. Suggestive features may include a pulmonary nodule, atypical region of consolidation with an alveolar pattern, cavitating lung mass, pleural effusion and pleural nodules, enlarged lymph nodes. Most will show features of mass or enlarged lymph nodes. Others include multiple nodes with cavitation due to necrosis of centrally located malignant tissue, mediastinal mass, features of consolidation

b) CT scan - This provides more definitive radiological criteria for a neoplastic lung lesion as well as staging of disease.

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

Tissue diagnosis

- Biopsy (obtained through bronchoscopy, mediastinoscopy, open biopsy etc)

- Fine Needle Aspirate cytology

- Sputum or thoracocentesis specimens can also 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 and 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.

LEPROSY

14

14.1 Introduction

14.1.1 Definition of Leprosy

Leprosy is an infectious disease caused by Mycobacterium leprae, an acid-fast, rod-shaped bacillus. The disease mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract, and the eyes. Leprosy is curable and treatment in the early stages can prevent disability.

14.1.2 Incubation period

The incubation period from infection to clinical manifestations is variable, it is shorter for Pauci bacillary (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.

KEY HIGHLIGHTS:

Introduction:

Leprosy is an infectious bacterial disease caused by Mycobacterium Leprae. It is an Acid-fast-rod shaped bacillus. It is classified into two:

1. **Pauci-bacillary leprosy (PB):**
   - Patients with 1 to 5 hypo pigmented patches
   - Skin slit smears negative
2. **Multibacillary leprosy (MB)**
   - Have more than 6 patches Skin smear often positive

Incubation period for Pauci-bacillary is between 2-5 years and Multi-bacillary between 5-10years. It is a slow multiplying bacillus.

Cardinal signs for Leprosy

- Hypopigmented/reddish skin patch/ lesion with loss of sensation
- Enlarged one of more peripheral nerve
- Presence of acid-fast bacilli in a slit-skin smear.

Treatment with Multi drug Therapy (MDT)-New update

Treatment of leprosy include use of 3 drugs regimen in all Leprosy patients.

- Monthly Rifampicin for 6 months in PB and 12 months in MB patients
- Daily Clofazimine for 6 months in PB and 12 months in MB patients
- Daily Dapsone for 6 months in PB and 12 months in MB patients

NOTE: Rehabilitation of patients with leprosy should form a key component in management and special consideration should be taken when the Eye is involved.

14.1.3 Source of Infection

The main source of infection is usually untreated Multi bacillary leprosy patients who are discharging bacilli via droplets from nose, mouth, during close and frequent contact.

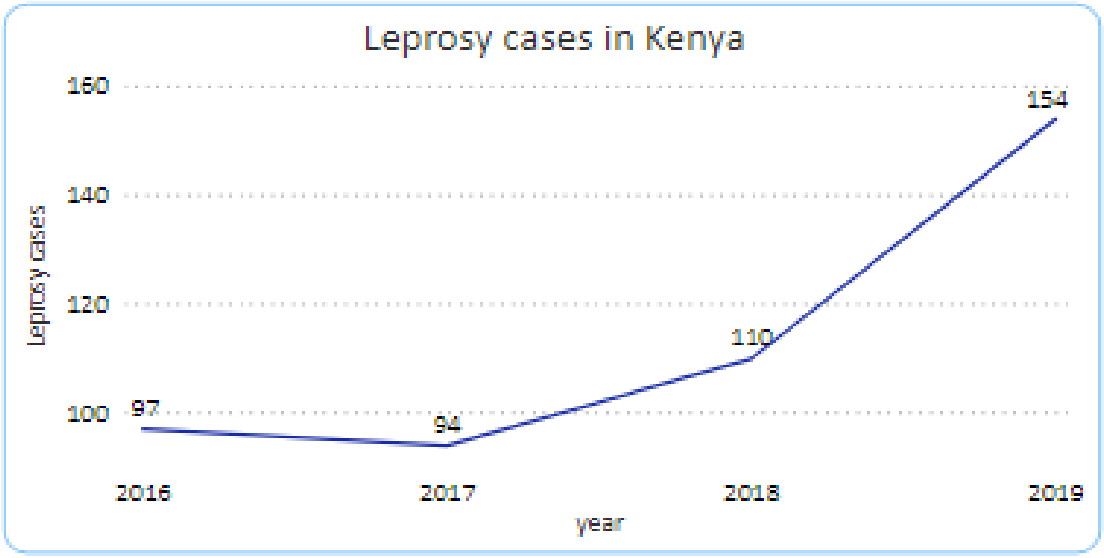
14.2 Background

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 books. However, the description in these books may include other dermatological conditions with similar manifestations.

Globally 208,619 cases of leprosy were reported in 2018 from 127 countries with the majority of leprosy patients being found in South East Asia, Americas and Africa. In the same year, Kenya reported 110 cases (80% were Multibacillary cases), of the cases notified 57% were male and only 2.7% were in the age group of 0-14 years indicating that we could be missing cases in this age group. In the last 3 years Kenya has reported an increased trend in leprosy cases among children under 15 years which is an indicator of ongoing transmission in the community.

Kenya has had an upward trend of cases from 97 in 2016, 94 in 2017,110 in 2018 to 154 cases in 2019. Currently the majority of leprosy cases are reported in the following counties in Kenya: Kilifi, Kwale, Homabay, Kisumu, Siaya and Busia. Despite efforts to control leprosy cases, Kenya is still in the post elimination phase (point preference below 1/10,000 population).



Population Affected

Leprosy affects persons in all age groups and both sexes. In Kenya the age group mainly affected is those above 65 years old contributing to about 25% of the total cases. Factors related to low socioeconomic status increase the risk of developing the disease.

14.3 Mode of transmission and risk factors

Transmission of leprosy is poorly understood, the exact route of *transmission* for leprosy is still uncertain at the present time. However, the inside lining of the nose and the mouth is thought to be the main route through which the leprosy bacteria enter the human body –the main **portal of entry**. When an untreated leprosy patient coughs or sneezes, the droplets of mucus containing the Mycobacterium leprae (M.leprae) bacteria are expelled into the air and can be inhaled by a susceptible person. Leprosy has a reservoir in armadillos and a few other animals.

Up to 95% of patients exposed to M. leprae will not develop the disease, suggesting that host immunity plays an important role in disease progression and control.

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.

14.4 Pathophysiology

The bacilli enter the body through the respiratory system by inhalation from an infected individual. It invades the coolers areas of the body which are the skin, mucous membranes and the peripheral nerves.

It has low pathogenicity where about 5% of infected people will develop signs and symptoms of the disease. After entering the body, the bacilli migrate towards the neural tissue and enter the Schwann cells. The bacteria can also be found in macrophages, muscle cells and endothelial cells of blood vessels.

After entering the Schwann cells /macrophage the progress depends on the immune status of the infected individual. The bacilli are slow in replication i.e. it takes about 12-14 days for one bacterium to divide into two within the cells. After replication it continues to affect more cells and up to this stage a 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 while the lymphocytes and histiocytes (macrophages) invade the infected tissue. The bacteria do not produce any toxin, but induces inflammatory reactions that lead to injury of the nerve and consequent disability. Damage can occur to one or more of the three components of the peripheral 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 and or hypopigmented 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.

14.5 Clinical presentation of disease

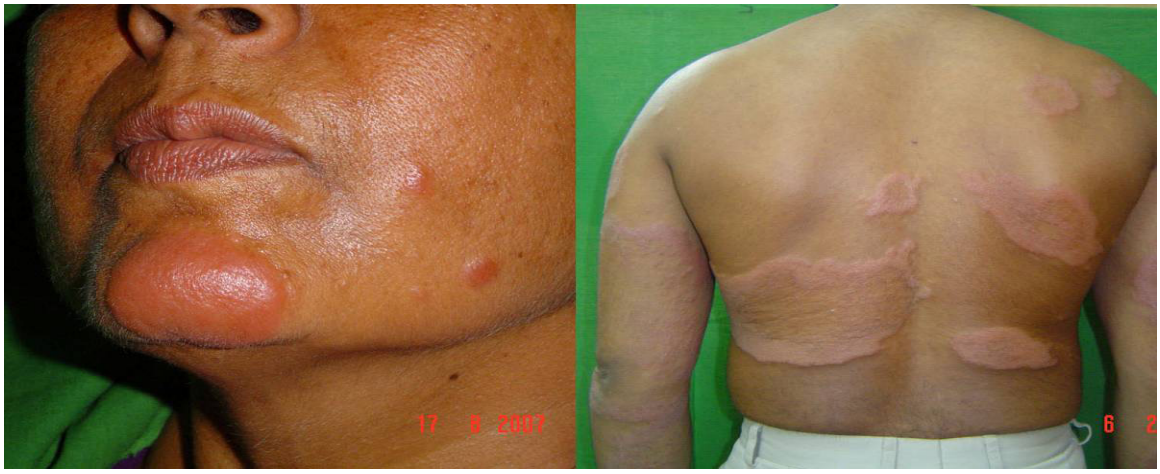
The case definition for Leprosy is a person with clinical signs of leprosy who requires chemotherapy (MDT).

Leprosy should be suspected in people with any of the following symptoms or signs:

- Pale/hypopigmented or reddish patches on the skin (the most common sign of leprosy)
- Loss, or decrease sensation in the skin patch
- Numbness or tingling of the hands or feet
- Weakness of the hands, feet or eyelids
- Painful or tender nerves
- Swellings or lumps in the face or earlobes
- Painless wounds or burns on the hands or feet

Although the majority of leprosy patients have straightforward skin lesions which are easy to see, experienced health care workers know that there is a great variety in the skin lesions of leprosy. Some skin lesions are very diffuse and difficult to distinguish from normal skin: in these cases, the other symptoms and signs become important.

Hypopigmented/reddish patch with loss of sensation



14.6 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. It is diagnosed clinically by finding at least **ONE** of the following cardinal signs by WHO classification:

(1) Definite loss of sensation in a pale (hypo pigmented) or reddish skin patch;

(2) Thickened or enlarged peripheral nerve, with loss of sensation and/or weakness

of the muscles supplied by that nerve;

(3) Presence of acid-fast bacilli in a slit-skin smear.

Physical examination

This should be conducted in a room with good lighting. A thorough review of the systems should be done however the following systems should specifically be reviewed.

1. Skin

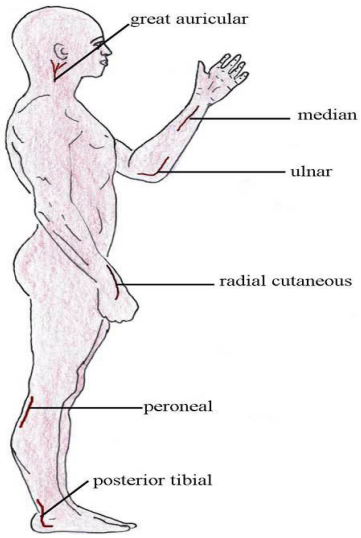
Look for hypo pigmented skin patches with loss of sensation using cotton wool to conduct a light touch. Examine for nodules, look for dryness cracks and hair loss on the patches and the eye brows lashes. Examine for muscle wasting. Ask the patient about skin discoloration and duration of its presence, presence and duration of nodules.

2. Nervous and Musculoskeletal system

Systematically examine the peripheral nerves for nerve enlargement tenderness and loss of function (autonomic, sensory and motor). Assess for weakness of muscles of hands, feet and eyes as well as loss of sensation in these parts and unnoticed injuries in the hands, feet and eyes

The following peripheral nerves are usually affected with different consequences and must be examined.

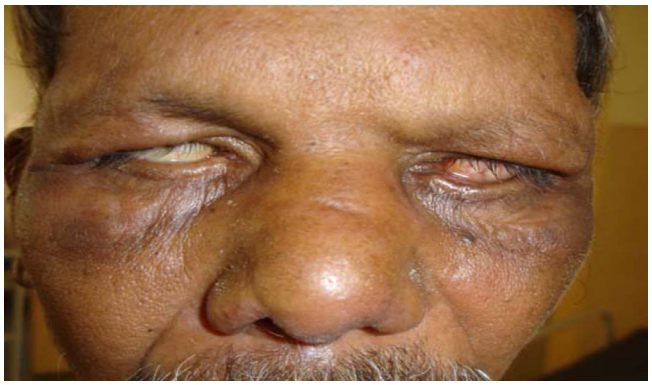
Figure 14.6.1 (Sites where peripheral nerves can be palpated)



a. Facial Nerve

Facial nerve damage leads to facial palsy (weakness in the muscles of the face). Facial palsy in leprosy it involve upper part of face due to selective involvement of zygomatic branch of facial nerve by leprosy lesion.

When the orbital branch is affected the patient will present with difficulty in closing the eyes (lagophthalmos (rabbit-like eyes).

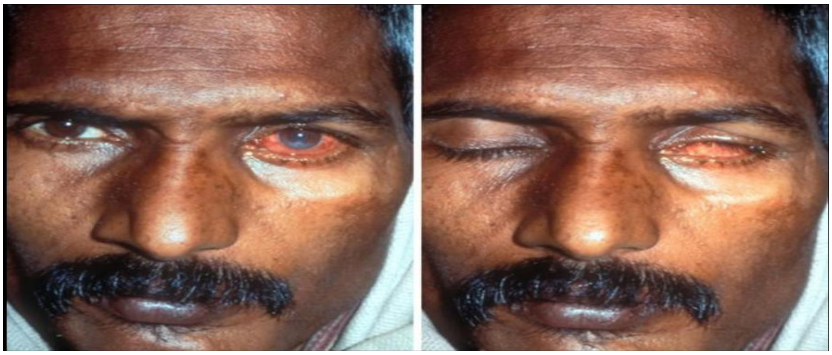


Lagopthalmos

b. Trigeminal Nerve

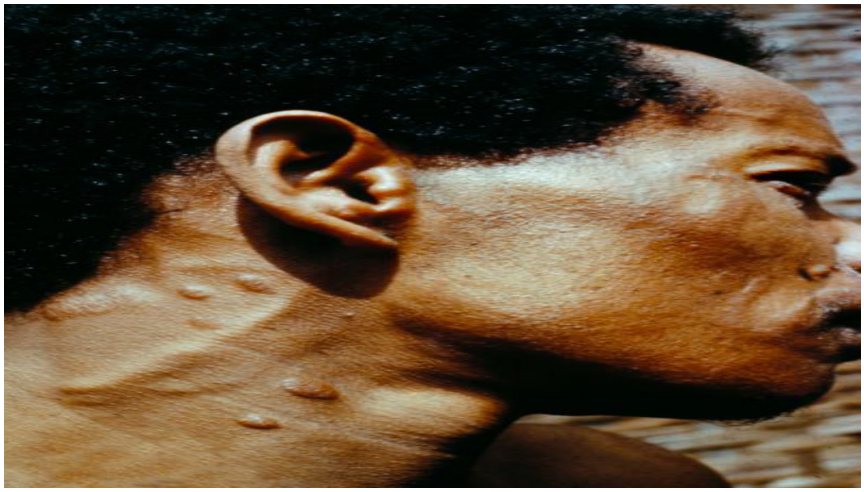
Damage to the trigeminal nerve leads to loss of the blink reflex resulting dryness and exposure keratitis. While examining the patient, observe for blinking.

The damage causes loss of sensation of the cornea leading to frequent injuries of the cornea by foreign objects. This may result in infection, healing with fibrosis, opacity formation and blindness. The eyes should always be examined for injuries.



c. Great Auricular Nerve

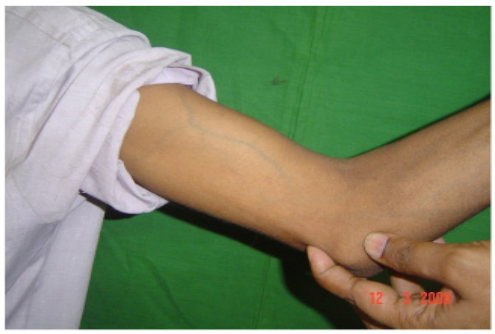
The nerve usually runs across the neck. In leprosy the nerve enlarges and a firm rod-like structure may be seen and felt under the skin. There is usually no obvious loss of function. The enlargement of this nerve is almost confirmation of the presence of leprosy.

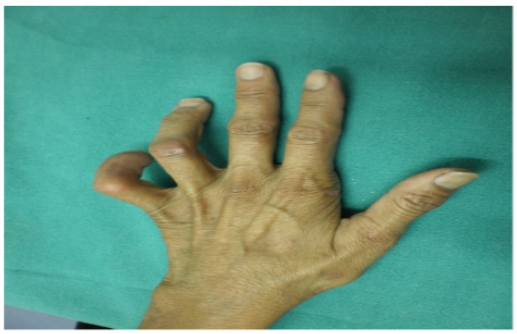


d. Ulnar nerve

The nerve runs in the olecranon groove in the medial aspect of the elbow joint. When damaged it leads to dryness in the hypothenar 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 hypothenar eminence and clawing of the fourth and the fifth fingers. The ulnar nerve also supplies the intrinsic muscles of the hand. Therefore, damage results in ridging of the hand due to muscle wasting.

Palpation of ulnar nerve





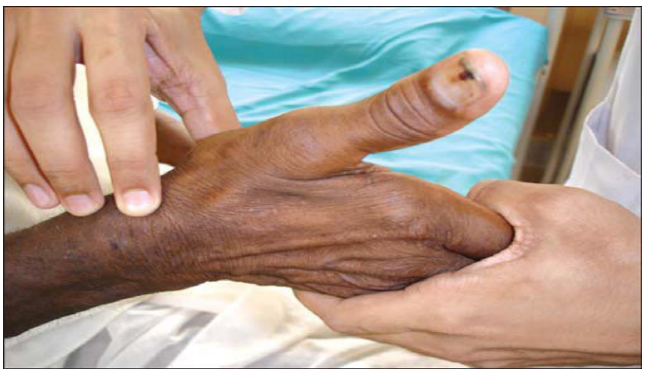
e. Median Nerve

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 manifests 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 ulnar nerve damage. Wasting of the thenar eminence leads to loss abduction resulting in ape thumb and clawing of the thumb 2nd and 3rd fingers.

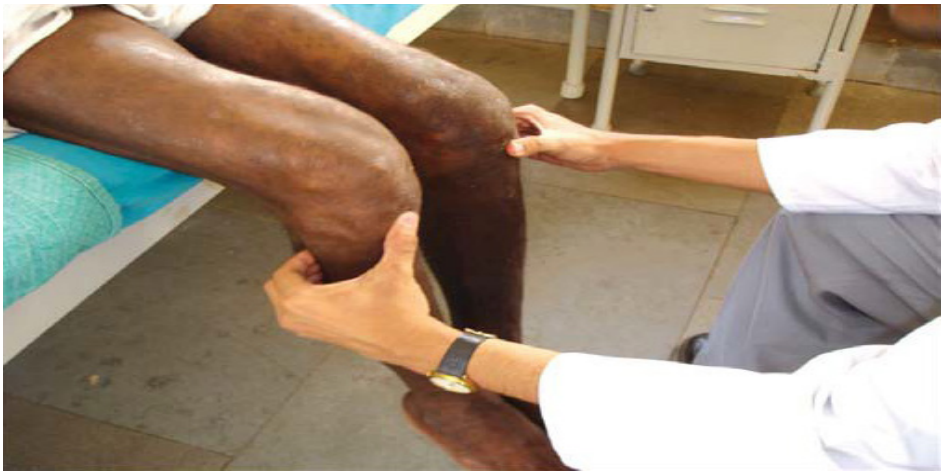
f. Radial Cutaneous Nerve

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.



g. Common Peroneal Nerve (lateral popliteal)

The common peroneal nerve can be felt just below the head of fibula below the knee arising from the popliteal fossa. This nerve is responsible for dorsiflexion and eversion of the foot. When damaged it leads to plantar flexion and inversion of the foot (foot drop). Observe the patients for evidence of foot drop while walking.



h. 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).

14.7 Laboratory Diagnosis of Leprosy

The diagnosis of leprosy is mainly clinical, however Leprosy can also be diagnosed in the lab (not a mandatory test), where in doubt.

These following diagnostic methods are used in leprosy diagnosis:

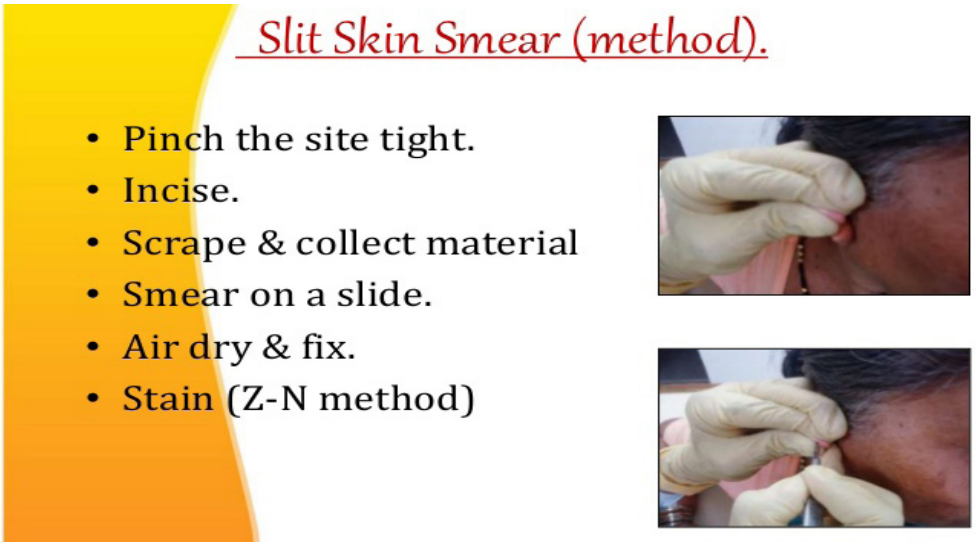
1. Bacteriological
2. Histological
3. Molecular methods

1. Bacteriological

a. Slit skin smears

Smears can be taken from any area of the body that manifest leprosy like a patch a nodule area of anaesthesia or infiltration. In practice smears are commonly taken from ear lobes, one elbow, and a contralateral knee.

Slit skin smear Procedure is as follows:



NB- *use gloves and ensure aseptic procedure.*

b. *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.

2. Histology

Skin or nerve biopsies can be taken for histological examination using various histological techniques like, ZN, FITES, etc.

3. Molecular techniques

Molecular techniques can be used to detect genetic materials of M.leprae for example PCR.

14.8 Differential Diagnosis

14.8.1 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 Lesions (Macules)**	
1. ***Birthmarks (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.
2. ***Vitiligo or Leucoderma***	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 hypo pigmented and can be confused with indeterminate leprosy. There is no sensory deficit in the patches.
3. ***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.
4. ***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 Hypo pigmented Lesions: (Papules / Plaques/ Nodules)**	
1. ***Seborrheic Dermatitis***	The lesions are yellow in colour and show coarse parakeratosis scaly lesions which are common on the chest and back and they may coalesce into larger polycyclic patches healing in the centre. Itching is usually mild.
2. ***Tinea Corporis***	These lesions, generally known as "Ringworm", are 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.

3. Psoriasis	Silvery white patches of psoriasis have no sensory loss.
4. 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.
5. Multiple Neurofibromatosis	Characterized by growth of non-cancerous tumours in the nervous system. The commonest tumours are acoustic neuromas. The most Common signs include hearing loss, ringing in the ears (tinnitus) and problems with balancing. Some people may develop cataracts.
6. Diabetic ulcers	This can often be confused with ulcers following neglected leprosy
14.8.2 Differential Diagnoses relating to nerves	
1. 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.
2. Toxic Neuritis	Patients working in paint factories or other heavy metal industries dealing with lead, arsenic etc. may develop a leprosy-like anaesthesia and paralysis. Careful recording of case histories is essential.
3.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.
4.Traumatic Neuritis	A careful recording of case history may reveal physical injury to the nerve, perhaps through an accident.
5.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 glycosuria and hyperglycaemia.
6.Bell's Palsy	This condition results from Facial Nerve involvement causing facial paralysis and lagophthalmos.

14.9 Immunology of Leprosy

Not all leprosy infections result into development of leprosy disease. The occurrence is dependent on 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 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 defence cells, at the same time establishing an inflammatory reaction. Cell-mediated immunity is essential for the body's defences 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. 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 humans have this type of immunity however to 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 multi bacillary leprosy.

Immunological spectrum and classification of leprosy

Although immunity, in most cases, helps the body's defence 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 "Leprae 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 defence 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.

14.10 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 classifies leprosy into two groups for epidemiological and treatment reasons.

Pauci-bacillary leprosy:

- Patients with 1 to 5 hypo pigmented patches
- Skin smears negative

Multibacillary 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

Table 14.10.1 Differences between PB and MB Leprosy

	Paucibacillary (PB)	Multibacillary (MB)
Previously called	*Tuberculoid Leprosy*	*Lepromatous Leprosy*
Severity	Mild	Can be extreme (Without treatment, the patient will die)
Unique Signs and Symptoms	Significantly milder with skin lesions and peripheral nerve enlargement as the only usual signs, possibility of spontaneous recovery	Lion-like face due to inflammation (**leonine facies**), as well as nasal cartilage damage causing **saddle-nose deformity**, **blindness** due to scarring of the eye can result, **infertility** may result in men
Distribution of lesions	Asymmetrical	Symmetrical
Occurs When	Infected person is **able** to mount a robust, cell-mediated immune response to the bacterium	Infected person **unable** to mount a cell-mediated immune response to the bacterium
Defined by World Health Organization as	1-5 patches associated with leprosy	>5 patches associated with leprosy
Is the person Infectious?	No	**Possibly**; bacterium is found in high concentrations in respiratory secretions and organs, but it is not clear how it is spread to another person

Prospects for Recovery	Good	Cure from disease possible, however, underlying disease complications (such as limb damage due to infection) may not be reversible or require reconstructive surgery

14.11 Disability Grading

Leprosy is graded by assessing the feet, hands and the eyes as follows;

14.11.1 Hands and feet

Grade 0: no anaesthesia, no visible deformity or damage.

Grade 1: anaesthesia present, but no visible deformity or damage.

Grade 2: visible deformity or damage present.

14.11.2 The eye

Grade 0: No eye problem due to leprosy; no evidence of visual loss.

Grade 1: Eye problems due to leprosy present, but vision not severely affected as a result of these (vision: 6/60 or better; can count fingers at 6 m).

Grade 2: Severe visual impairment (vision: worse than 6/60; inability to count fingers at 6 m) also includes lagophthalmos, iridocyclitis and corneal opacities.

14.12 Leprosy Management

14.12.1 Chemotherapy

There are 3 first line drugs used in leprosy management; Rifampicin, Clofazimine and Dapsone.

Figure 14.12.1 (2018 WHO Leprosy Treatment Guidelines.)

Age Group	Drug	Dosage and frequency	Duration	
			MB	PB
Adult	Rifampicin	600 mg Once a month	12 months	6 months
	Clofazimine	300 mg once a month and 50 mg daily		
	Dapsone	100 mg daily		
Children (10-14 years)	Rifampicin	450 mg Once a month	12 months	6 months
	Clofazimine	150 mg once a month, 50 mg on alternate days		
	Dapsone	50 mg daily		

Children <10 years old or <40 kg	Rifampicin	10 mg/kg once a month	12 months	6 months
	Clofazimine	100 mg once a month, 50 mg twice weekly		
	Dapsone	2 mg/kg daily		
Note; *The treatment for children with body weight below 40 kg requires single formulation medication since no MDT combination blister packs are available for children between 20 and 40 kg, It would be possible to follow the instructions of the operational manual, Global leprosy strategy 2016-2020 on how to partly use (MB-child) blister packs for treatment (60)*				

14.12.2 Common Drug Side Effects and Management

1. Dapsone

- *Slighting itching (Dapsone syndrome)*

Reassure patients and treat symptomatically with an antihistamine.

- *Anaemia*

Investigate for other causes of anaemia, and manage appropriately/ refer to a 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 a medical officer or SCTLC or nearest hospital.

- *Fixed drug reaction*

Stop drugs, the eruption will slowly clear after stopping.

2. Clofazimine (Laprene)

- *Gastrointestinal disturbances nausea, vomiting, abdominal pains.* Give drugs after a 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

- *Hyperpigmentation/darkening of the skin*

3. 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*

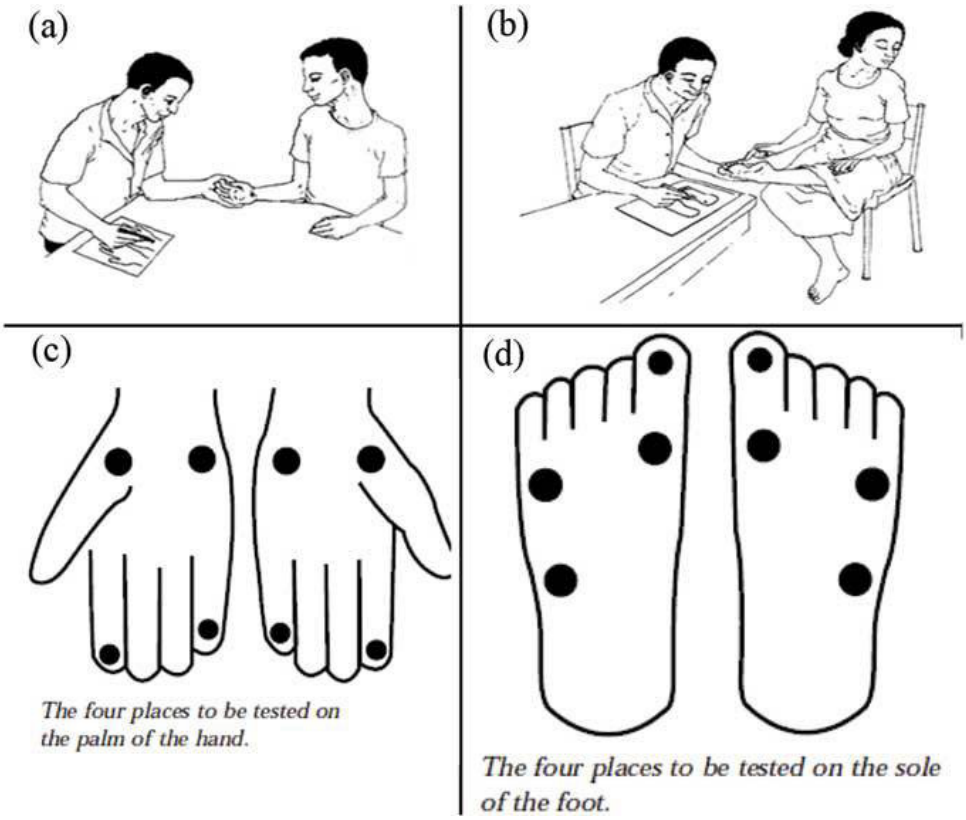
Investigate for other causes of anaemia, manage appropriately/ refer to medical officer or SCTLC for further management.

14.13 How to Conduct a Voluntary Muscle Testing and Sensitisation Test (VMT/ST)

14.13.1 Sensation in hands and feet

Check the sensation in the palms of the hands and the soles of the feet, using a ballpoint pen:

- Explain the test to the patient
- Ask them to close or cover their eyes
- Touch the skin very lightly with the ballpoint
- Ask the patient to point to the place you touched
- Test a minimum of four points on each hand and foot
- Note any areas where the pen is not felt.



The four places to be tested on the palm of the hand.

The four places to be tested on the sole of the foot.

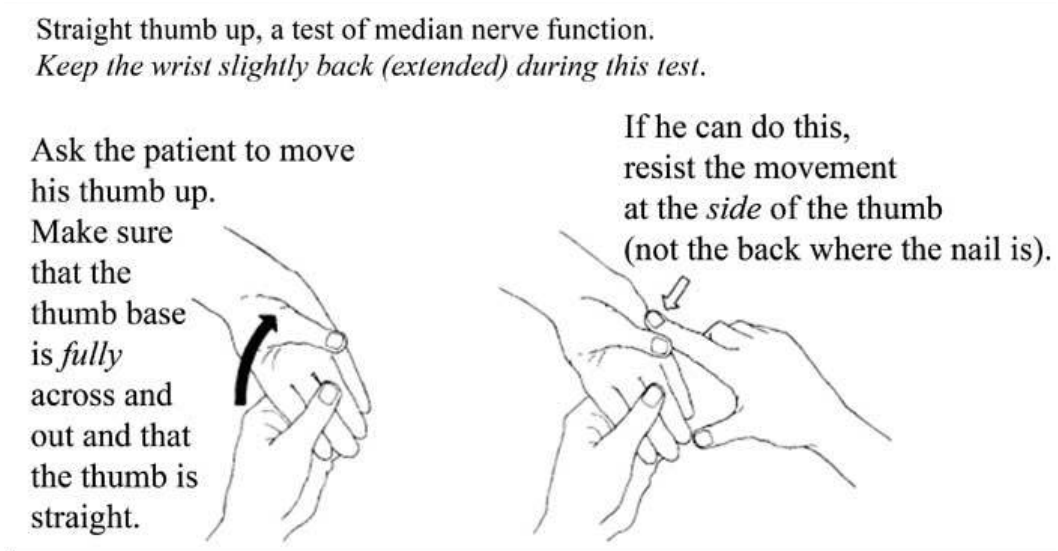
NB: In the palm of the hand, the side with the little finger is supplied by the ulnar nerve. The part with the thumb, index and middle fingers is supplied by the median nerve. The sole of the foot is supplied by the posterior tibial nerve.

14.13.2 Check for Muscle Weakness

Examination of hands and feet for muscle weakness

1. Thumb up (tests the median nerve)

- Ask the person to put out their hand, palm up
- Support their hand in your hand
- Ask them to point the thumb towards their own nose
- Test the strength of the thumb to stay in that position.



2. Wrist back' test of radial nerve function

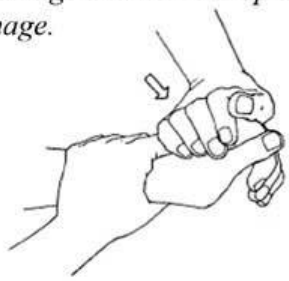
Below figure shows the test for radial nerve function. Again, you are testing for how much resistance there is to pressure you apply, this time to the individual's raised hand, while you support the wrist.

1 Is movement full? 2 Is resistance full?

Wrist back: a test of radial nerve function

This test is sometimes omitted from simple record forms, as radial nerve damage is rare. Where radial nerve damage and nerve drop do occur they usually follow median nerve damage.

Ask the patient to pull his wrist back fully.
Support the patient's wrist.



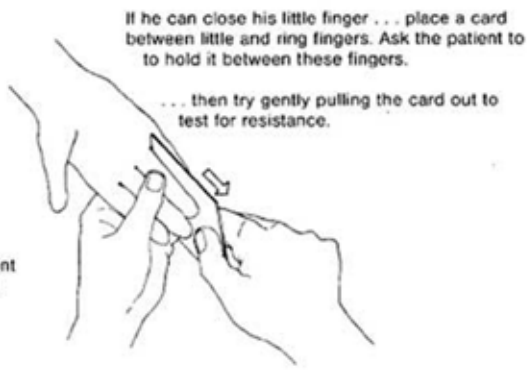
Press gently but firmly at the back of the hand to test for resistance.

3. Little finger out (tests the ulnar nerve)

- Ask the person to put out their hand, palm up
- Support their hand in your hand
- Ask them to move the little finger out
- Test the strength of the little finger to stay in that position

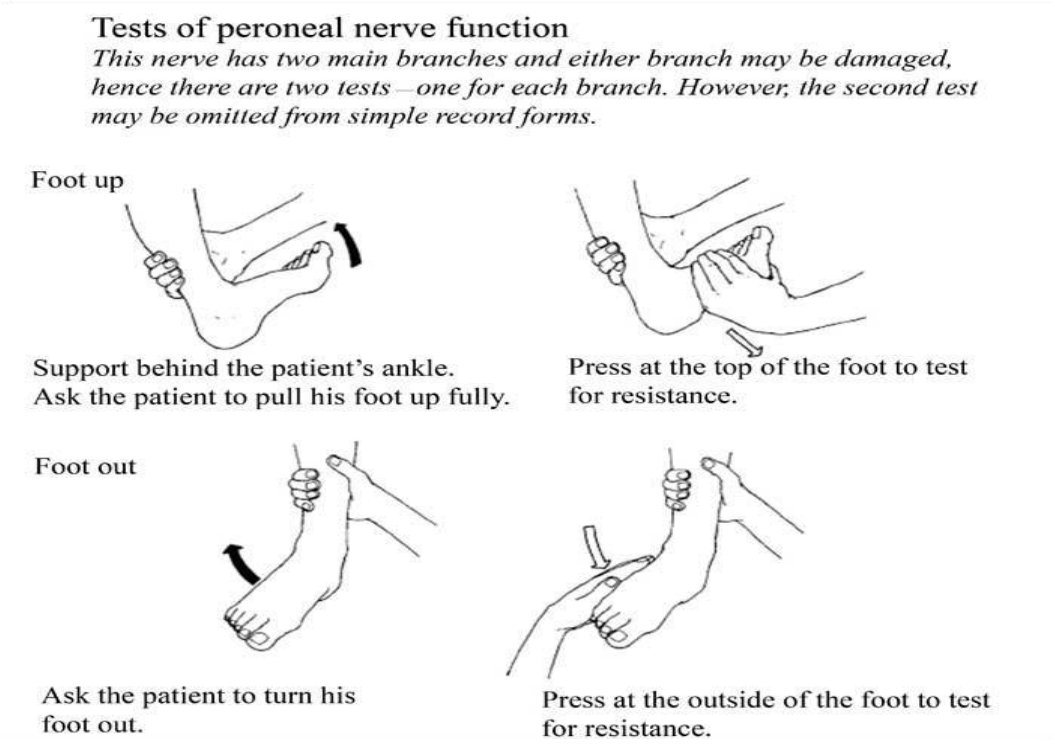
1 Is movement full? 2 Is resistance full?

Little finger in... a test of ulnar nerve function



4. Foot up' test of peroneal nerve function

The movement of the foot is due to muscles activated by the peroneal nerve and the test for muscle power in this case is shown below. You apply pressure to the top of the raised foot by trying to push it down. Can the person still lift up the foot against your pressure?



By testing the strength of the voluntary muscles (which means the muscles we can move at will, e.g. in our arms and legs), you can find out if the person's nerve function is normal, or has been weakened or paralyzed by leprosy. The findings are recorded as follows:

- *Paralyzed* (P): the muscle has lost all strength and cannot produce any movement;
- *Weak* (W): there is some movement, but muscle strength is reduced;
- *Strong* (S): the muscle strength is normal.

14.14 Management of Leprosy Complications

14.14.1 Leprosy Reactions

This results from an 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.

Figure 14.14.1: Management of Leprosy reactions

Type	Category	Occurrence	Management
Type 1 reactions	Mild type 1 reactions,	On skin only; there may be mild fever and slight swelling (edema) of the limbs.	Baseline VMT/ST-(explain how to do this), paracetamol 2 tablets TDS for 1 week and review after 1 If there is deterioration to moderate or severe, treat as recommended
	Moderate type 1 reactions	A number of skin patches are involved, some of the nerves are enlarged and tender but no evidence of loss of function.	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 reactions	Most of all the skin patches are affected, A number of nerves are enlarged, tender, with evidence of loss of nerve function	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
Type 2 reaction	Mild type 2 reactions	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 actappropriately
	Moderate type 2 reactions	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 reactions	generalized ENL, high fever (30-40oc) 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 reactions		Treatment requires reinitiating 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 a duration of 4 months

Note for severe type 1 reaction; *If there is no response or no changes in the VMT/ST. The treatment has failed, Wean the patient off Prednisolone by reducing to 15mg OD for 2 weeks, 10mg OD for 2 weeks and 5mg OD for 2 weeks, Assess for reconstructive surgery, rehabilitation and health education on the care of the eyes, hands and feet, At 20mg OD 6 weeks, and after 6 weeks of prednisolone, VMT/ST still shows improvement in nerve function, Continue with 20mg Prednisolone daily and 2 weekly VMT/ST until you get 3 readings of VMT/ST that are similar, Reduce Prednisolone to 15mg OD for 2 weeks, 10mg OD for 2 weeks and 5mg OD for 2 weeks.*

14.14.2 Differential diagnosis of leprosy reaction

- *Drug 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 hyperpigmentation.

- *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.

14.14.3. Factors predisposing to leprosy reaction

1. *Ant leprosy treatment*: improved immunity & Ag-Ab complexes.
2. *Inter current infection:* disrupt immunological balance between bacilli and host.
3. *Physiological factors:*
   - Stressful conditions due to stigma.
   - Pregnancy.
   - Puberty in males due to hormonal changes.

14.15 The Eye in Leprosy

The eye is affected in leprosy in 2 main ways:

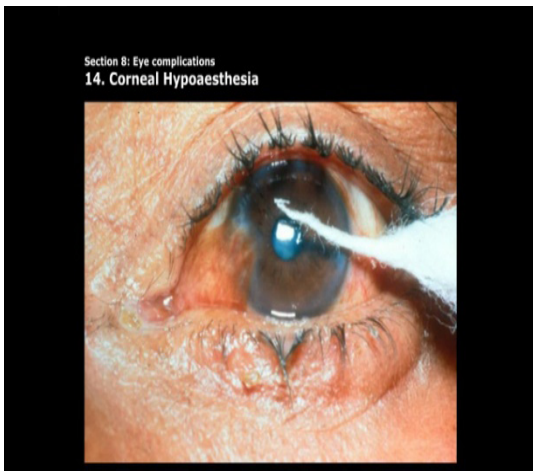
1. Direct bacillary invasion
2. Leprosy reactions.

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.

14.15.1 Examining the eyes and eyelids

Testing for corneal sensation

Cornea is very sensitive to being touched in a healthy person, who will blink if something touches it. Corneal sensitivity is lost in a person with leprosy. Observe the person's blink when talking to him/her. If the blink is normal, corneal sensation will be normal and there is no need for the test. If there is no blink, the eye is at risk.



14.15.2 Management: initiation of MDT

- **Type 1 reaction in the eye**

Type 1 reactions: facial nerve damage leads to inability to close the eye (lagophthalmos).

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 orbicularis 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 ciliary 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.

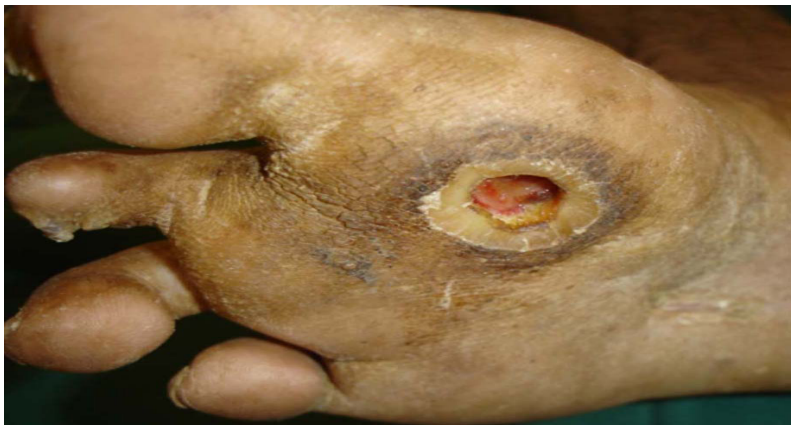
Signs and symptoms of Iridocyclitis

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 Iridocyclitis

- Iridocyclitis: Initial care: Instil 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 making them shorter thus reducing the risk of attachment.

14.16 Foot Care in Leprosy



- Regular check-up of sensation of the foot
- Regular soaking of the foot and applying petroleum jelly on the foot
- Surgically remove any dead tissues from the wound
- Avoid walking bare-footed
- Use of MCR sandals- this footwear has a tough outer sole, should not rub against toes. Where unavailable advise them to get appropriate footwear which has an outer sole of 15-18mm thick and soft inner sole 18-22mm.
- Use normal fitting shoes
- Encourage bed rest and elevate foot in the acute phase
- Remove slough or other draining procedures.

14.16.1 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.

14.17 Common Deformities & Disabilities

1. Madarosis- loss of eyebrows and eyelashes
2. Lagophthalmus- leads to inability to close and open the eye voluntarily.
3. Collapsed nose (saddle nose)- leads to poor breathing in and out
4. Wrist drop – inability to extend the wrist
5. Ape thumb- leads to no thumb opposition and abduction
6. Claw hand – inability to flex the proximal metacarpophalangeal joint of the 4^{th} and 5^{th} fingers and inability to extend the distal metacarpophalangeal joints of these fingers
7. Foot drop – inability to dorsiflexion and evert the foot
8. Claw toes – leads to injuries to the metatarsal heads and toes
9. Plantar ulcers.

14.18 Health Education to Patients on Leprosy

1. To take the drugs after a meal or in the evening just before going to bed if he feels nausea after ingesting them
2. To inform the staff at the clinic if they intend to travel or move to another area
3. Tablets given are to be taken daily at the same time.
4. Drugs to be collected from the clinic every four weeks
5. Leprosy reactions can still develop after M.D.T. the reaction should not be treated with a new course of MDT but other drugs will be used to treat them
6. Skin discoloration due to clofazimine
7. Urine discoloration due to rifampicin
8. When to report to the clinic as soon as he notices; -
    - Sudden weakness of muscles
    - One or both of his eyes are red and painful.
    - Pain in one of his limbs
    - The appearance of red, swollen tender nodules in the skin.
    - And as soon as patches have started to become red and swollen again.

14.19 Special Cases and their Treatment

1. 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.

2. Treatment for patients also infected with HIV

Patients infected with HIV usually respond equally well to leprosy treatment as those without HIV infection.

3. 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.

4. Leprosy and Malnutrition

(For further information, refer to the nutrition section in main document)

- Do Nutritional assessment
- Manage as per nutritional interventions
- Vitamin A- at the start and at completion of leprosy treatment
- Pyridoxine- Given to those with peripheral neuropathy throughout the treatment period
- Give food supplements if the BMI is <18.5manage as per the nutrition intervention schedule.
- BMI of >18.5 provide nutritional counselling to the client.

14.20 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 misclassification and has to start MB treatment.

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.

NB: Leprosy relapse should not be confused with leprosy reaction. In relapse PCR and slit skin smears will be positive while in reaction they will be negative.

Figure 14.20.1: Drug resistance leprosy

Area of the recommendation	Recommendation
Treatment of drug-resistant leprosy	Leprosy patients with rifampicin resistance may be treated using at least two of the following second-line drugs: clarithromycin, minocycline or a quinolone (ofloxacin, levofloxacin or moxifloxacin), plus clofazimine daily for 6 months, followed by clofazimine plus one of the second-line drugs daily for an additional 18 months. Leprosy patients with resistance to both rifampicin and ofloxacin may be treated with the following drugs: clarithromycin, minocycline and clofazimine for 6 months followed by clarithromycin or minocycline plus clofazimine for an additional 18 months.
Prevention	
Chemoprophylaxis for contacts of patients with leprosy	Single-dose rifampicin (SDR) may be used as leprosy preventive treatment for contacts of leprosy patients (adults and children aged 2 years and above), after excluding leprosy and tuberculosis (TB) disease, and in the absence of other contraindications. This intervention shall be implemented only by programmes that can ensure: (i) adequate management of contacts, and (ii) consent of the index case to disclose his/her disease.

14.21 Rehabilitation

1. 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.

2. 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.
- Link them with disability programs at the County level

3. Spiritual

- It helps in reducing stigma
- Encourage them to join their religious bodies of their choice

4. Surgical

This involves surgical procedures to correct the deformities:

- Madarosis: Hair grafting
- Lagophthalmos: Tarsorrhaphy &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,
- Sequestrectomy,
- Amputation,
- Orthopaedic appliances
- Footwear: normal tyre sandal with micro-cellular rubber (MCR). Refer patients with footwear needs to the rehabilitative department.

14.21.1 Prevention of Leprosy

a) Chemo-prophylaxis- for close contacts is offered in high burden countries.

b) 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 diagnosis, Prompt and adequate treatment.

14.22 Leprosy Active Case Finding

The following intervention can be used to increase active case finding for leprosy:

1. Training and sensitization of health care workers on leprosy diagnosis and care
2. Build the capacity of communities to suspect leprosy and refer suspected cases through Community health volunteers hence reducing stigma.
3. Counties to conduct polyskin clinics in the affected counties to identify the missing leprosy cases- invite all persons with dermatological conditions to come for medical check up
4. Actively conduct contact tracing for all leprosy patients diagnosed.

14.22.1 The role of community and community health volunteers in Leprosy care

1. Suspect and refer leprosy patients to the health facilities
2. Offer treatment support to leprosy patients
3. Support the leprosy patients to be integrated in the community
4. Assist in defaulter tracing/ retrieval
5. Support the leprosy patients in rehabilitation and wound care
6. Participate in health education meetings
7. Resource mobilization
8. Mobilise the community members to attend the poly skin clinic camps

14.23 Monitoring and Evaluation

Key indicators for monitoring progress

1. Case notification rate- Total Number of leprosy cases notified divided by the population per 100,000 in a given period.
2. Proportion of leprosy cases with grade 2 Disability detected
3. Proportion of children below 15 years detected
4. Proportion of children below 15 years with grade 2 Disability detected
5. Proportion of MB cases among the new cases notified.

Treatment outcome indicators

1. Proportion of leprosy cases released from treatment- Number of leprosy cases who have been released from treatment divided by the total number of leprosy initiated on treatment
2. Proportion of leprosy patients lost to follow up- Number of leprosy cases lost to follow up divided by the total number of leprosy cases detected.
3. Proportion of leprosy patients who have died.

PHARMACOVIGILANCE

15

OBJECTIVES:

- **Striving for early detection of any adverse reactions and interactions.**
- **Identification of risk factors and possible mechanisms underlying adverse reactions.**
- **Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing and regulation.**

Definitions of terms

Pharmacovigilance

The science and activities related to enhancing the quality, safety and rational the use of medicines thereby improving patient care and public health. It involves the activities related to the detection, assessment, understanding, prevention and management of adverse effects or any other possible patient to medicine related problems.

Table 15.1: Pharmacovigilance definition of terms

Term	Definition
Adverse event (AE)	Any untoward medical occurrence that may present in a TB patient while undergoing treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with this treatment.
Adverse drug reaction (ADR)	A response to medicine that is noxious and unintended, including lack of efficacy and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine.
Causality assessment	The evaluation of the likelihood that a TB medicine was the causative agent of an observed adverse reaction.
Serious adverse event (SAE)	An AE which either leads to death or a life-threatening experience; to hospitalization or prolongation of hospitalization; to persistent or significant disability; or to a congenital anomaly. SAEs that do not immediately result in one of these outcomes, but which require an intervention to prevent it from happening are included. SAEs may require a drastic intervention, such as termination of the drug suspected of having caused the event.

Term	Definition
AE of special interest	AE documented to have occurred during clinical trials and for which the monitoring program is specifically sensitized to report regardless of its seriousness, severity or causal relationship to the TB treatment
AE of clinical significance	AE that is either serious (SAE) or of special interest that leads to a discontinuation or change in the treatment, or judged as otherwise clinically significant by the clinician
Signal	Reported information on a possible causal relationship between an adverse event and a TB medicine, the relationship being unknown or incompletely documented previously or representing a new aspect of a known association

Why Pharmacovigilance is Importance

Different brands of medicines may differ in the way they are produced and the ingredients that are used. Once marketed, the medicines are used by patients who have many different diseases or are using several other drugs and who have different diets which may affect the way in which they react to a medicine.

In order to prevent unnecessary suffering by patients and to decrease the financial loss sustained by the patient due to the inappropriate or unsafe use of medicines, it is essential that a monitoring system for the safety of medicines is supported by doctors, pharmacists, nurses and other health professionals in the country. The Pharmacy and poison board (PPB) are committed to improving drug safety through adverse drug reaction monitoring. Through PPB pharmacovigilance programme and national TB and Leprosy disease program (NTLD) adverse reactions should be reported daily.

All patient or their next of kin, health care workers, including doctors, dentists, pharmacists, nurses and other health professionals are requested to report all suspected adverse reactions to drugs especially when the reaction is unusual, potentially serious or clinically significant. It is vital to report an adverse drug reaction to the pharmacy and poison board Pharmacovigilance programme even if you do not have all the facts or are uncertain that the medicine is responsible for causing the reaction

Benefits of Pharmacovigilance

The objectives of PV are;

- To improve patient care & safety in relation to medicines & all medical & para-medical interventions
- To improve public health & safety in relation to the use of medicines
- To contribute to the assessment of benefit, harm, effectiveness and risks of medicines

- To promote understanding, clinical training & effective communication to health professionals & the public.

Pharmacovigilance will cover the following components

The major components are;

- Data collection and analysis
- Interventions / management report
- Reporting
- causality assessment.

Data collection and analysis

What to collect is vital into understanding the cause of adverse reactions and addressing the issues well. When a patient presents themselves at a facility, healthcare worker should have time to record the following;

1. Take a proper history and do a proper examination
    - A full drug and medical history should be done
    - Can this adverse be explained by other causes e.g. patient's underlying disease, other drug/s, over-the-counter medicines or traditional medicines; toxins or foods
    - It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is. A drug-related cause should be considered, especially when other causes do not explain the patient's condition
2. Establish time to understand the onset of drug reactions
    - Some reactions occur immediately after being given a medicine while other reactions take time to develop
    - The time from the start of therapy to the time of onset of the suspected reaction must be logical.
3. Do a thorough physical examination with appropriate laboratory investigations
    - Few drugs produce distinctive physical signs
    - Exceptions include fixed drug eruptions, steroid-induced dermal atrophy, acute extrapyramidal reactions
    - Lab tests are especially important if the drug is considered essential in improving patient care or of the lab test results will improve management of the patient
    - Try to describe the reaction as clearly as possible and where possible provide an accurate diagnosis

4. Effect of de-challenge and re-challenge should be determined. (when necessary)

   De-challenge = withdraw of drug

   - Resolution of suspected ADR when the drug is withdrawn is a strong, although not conclusive indication of drug-induced disease.
   - In cases where a withdrawal reaction is experienced, a de-challenge is when the drug is again given to the patient.
   - "Positive" de-challenge = improvement of reaction when de-challenge occurs

   Re-challenge = reintroducing the drug after a de-challenge.

   - This is only justifiable when the benefit of re-introducing the drug to the patient outweighs the risk of recurrence of the reaction. This is rare. In some cases, the reaction may be more severe on repeat exposure.

5. Check the known pharmacology of the Medicine.
   - Is the reaction known to occur with the drug as stated in the package insert or other reference?
   - If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that medicine.

6. Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.

Patient counselling

Medicine plays an important role in medical care. Effectiveness of treatment depends on both the efficiency of medication and patient adherence to the therapeutic regimen. Patient needs to be informed about potential ADRs and management strategies should any occur and advice to report any side effect immediately. Patient need to understand that sometime people not all can get ADRs when taking medicine and that ADRs vary from person to person. Most ADRs occur within the first few weeks of starting medication and then improve after a few weeks or months.

What do you do if you notice any side effects?

- If you develop any ADR return to the clinic immediately and discuss with your healthcare worker.
- If the side effects are mild then you can continue taking your medicines without missing any doses, and then discuss it with the clinician at your next appointment.
- If the side effects are bothering you too much then return to the clinic immediately, even if you do not have a scheduled appointment, to discuss what to do next; you can also call the clinic if you are not able to make it yourself immediately.

Reporting

Facilities are expected to report all ADRs, and side effects to pharmacist, CTLCs and SCTLCs for submission to PPB using the yellow forms through their website or email and to NTLDP for entry in TIBU (Chart on data and information flow). The adverse events and ADRs for DRTB to be recorded in the DRTB patient logbook and reported through aDSM/ADR reporting tool (in TIBU) and PPB ADR reporting form (yellow form) (annex 1)

- **Report all ADRs to PPB via the PPB website *(http://www.pv.pharmacyboardkenya.org/)* or via email *pv@pharmacyboardkenya.org***

  Where the website is not available;

  - **Fill out in the yellow form**
  - **Submit a hardcopy to the sub-county Pharmacist**

Methods of reporting in pharmacovigilance

a) **Spontaneous reporting** is the most common form of PV is spontaneous which involves a health-care worker - or even the patient - reporting a drug-related reaction. The effectiveness of this depends on the patient volunteering this information to health-care workers' competence to recognize an event, and their motivation to report it.

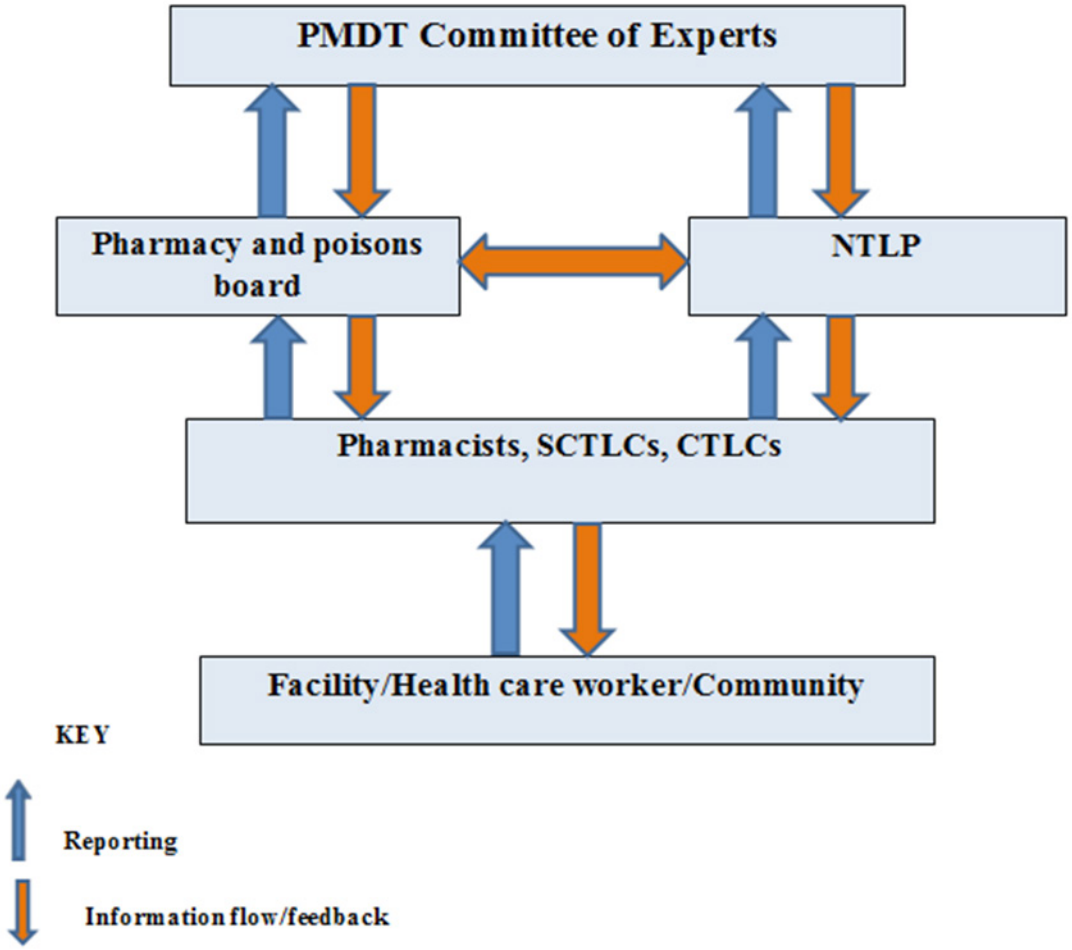
b) **Targeted spontaneous reporting** uses a methodology that monitors and records all or a specific set of safety concerns in a defined population of treated patients, e.g. drug resistant TB patients on treatment.

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. 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).

Information and data flow

The data received will be entered and analyzed at the National Pharmacovigilance Centre at the PPB, supported by the Expert Safety Review Panel (ESRP). 9. The Pharmacy and Poisons Board will review the reports received from all sources and advise on or take the appropriate action. 10. Feedback to all levels of the system will be the responsibility of PPB.

Figure15.2: The ADR information and reporting flow chart



ADRs reporting tools: Annex 1,2,3

- **Yellow form (PV 1)** - form to capture all suspected adverse drug reactions
- **White card (PV 4)** – Patient Alert card for life threatening drug reactions
- **Pink form (PV 6)** - form for reporting poor quality medicinal products

Causality assessment

In order to assess the likelihood that the suspected adverse reaction is due to the medicine, the WHO has provided a list of causality assessment criteria for deciding on the contribution of the medicine towards the adverse event. These criteria are defined as follows:

Certain: Clearly caused by the exposure**.** *There is **clear** evidence to suggest a causal relationship and other possible contributing factors can be ruled out.*

Assessment criteria;

- Clinical event, lab test abnormality with plausible time relationship to drug intake
- Cannot be explained by concurrent disease or other drugs /chemicals

- Response to withdrawal- plausible
- Event must be definitive pharmacologically / immunologically
- Positive rechallenges (if performed).

Probable/ Likely: Likely to be related to the exposure. *There is evidence to suggest a **likely** causal relationship and the influence of other factors is unlikely.*

Assessment criteria;

- Clinical event, lab test abnormality with reasonable time relationship to drug intake
- Unlikely to be attributed to disease, drugs / chemicals
- Clinically reasonable response to withdrawal (dechallenge)
- Rechallenge not required.

Possible: May be related to the exposure. *There is **some** evidence to suggest a causal relationship (because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant treatments).*

Assessment criteria;

- Clinical event lab test abnormality with reasonable time relationship to drug intake
- Could also be explained by disease or other drugs or chemicals
- Information on drug withdrawal may be lacking or unclear.

Unlikely: Doubtfully related to the exposure. *There is **little** evidence to suggest there is a causal relationship (the event did not occur within a reasonable time after administration*

of the study regimen). There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant treatment).

Assessment criteria;

- Clinical event, lab test with improbable time relationship to drug intake
- Other drugs, chemicals or underlying disease provide plausible explanations.

Condition/ unclassifiable: There is insufficient information about the ADRs to allow for an assessment of causality

Assessment criteria;

- Event or laboratory test abnormality
- More data for proper assessment needed, or
- Additional data under examination.

Unassessable / unclassified: There is insufficient information about the ADRs to allow for an assessment of causality and more ***is expected***.

Assessment criteria;

- More data is essential for proper assessment or additional data are under examination.

In most cases there is some level of uncertainty as to whether the drug is directly responsible for the reaction. Many of the questions above may remain unanswered or may be contradictory, however this should not dissuade you, from reporting the reaction to the {Pharmacy and poisons board and NTP}. A well-documented report which includes information about all the above-mentioned questions can provide us with the first signal of a previously unknown problem.

Roles and Responsibilities

The entire system of pharmacovigilance works with the support of each healthcare provider, the regulatory bodies, the pharmaceutical industry, other stakeholders and the public at large. Hence, each of these has an important role to play and responsibility to bear:

Patient / Public

Patients to report any unacceptable, unexpected or suspected adverse effect of medicine dispensed to them.

Health Care Worker

Patient awareness of possible serious reactions, and development of a culture to report reactions to clinics, will be essential for any pharmacovigilance system. Health facility staff provides an essential link in the detection of ADRs at the periphery of the healthcare system. The healthcare worker's roles in the PV system are:

- Patient education
- Detection and appropriate clinical management
- Reporting
- Documentation- to maintain accurate documents
- Investigation, where necessary
- Patient feedback.

Hospital pharmacist

- Receive reports from the healthcare workers in the hospital and send them to the sub county pharmacist.
- Review the patients` ADR prognosis and interventions.
- Develop a pharmaceutical care plan for the patient (PCP).
- Generate a drugs utilisation review report.

- Manage the Hospital pharmacovigilance budget.
- Chair the hospital pharmacovigilance committee.
- Member of the clinical view meetings in the Hospital/Facility.

Clinical pharmacist specialist

- Initiate immediate short-term interventions of the ADRs.
- Review the patients` ADR prognosis and interventions.
- Develop a pharmaceutical care plan for the patient (PCP).
- Conduct therapeutics drugs monitoring reports (TDM).
- Manage the MTM clinic and TDM budget.
- Coordinate facility medicines based operational research and clinical trials.
- Chair the drugs utilisation review reports.
- Training of the healthcare staff.
- Member of the clinical review meetings in the hospital.

Sub County Pharmacist

- Receive reports from health centres and send ADR reports from district to PPB on a monthly / weekly basis or on an ad hoc basis in an emergency.
- Initiate immediate short-term interventions of the ADRs.
- Coordinate the sub county reviews of the patients` ADR prognosis and interventions.
- Coordinate the pharmaceutical care plans for the patient (PCP) reviews for the sub county. Coordinate the therapeutics drugs monitoring reports (TDM) reviews in the sub county.
- Facilitate investigations for causality assessment, initiated by PPB, where necessary.
- Training of healthcare staff in facilities.
- Member of the clinical review meetings for TB in the sub county.

County Pharmacist /Pharmacovigilance pharmacist specialist

The pharmacovigilance important roles of the county pharmacist (assisted by Pv pharmacy specialist/clinical Pharmacist) are:

- Coordinate all activities of pharmacovigilance in the county
- Training of healthcare staff in the county.
- Facilitate investigations for causality assessment, initiated by PPB, where necessary.

- Manage and coordinate the Pharmacovigilance implementation and coordination budget in the county.
- Chair the county Pharmacovigilance committees.
- Chair the county commodities security meetings.
- Coordinate the County reviews of the patients` ADR prognosis and interventions.
- Coordinate the pharmaceutical care plans for the patient (PCP) reviews for the county. Coordinate the therapeutics drugs monitoring reports (TDM) reviews in the county.
- Coordinate MTM clinic activities in the county.
- Provide policy and regulatory interphase between the county and the program and PPB respectively.
- Member of the county clinical review meetings in TB.

Clinical Review Team

The clinical review team plays a central role in monitoring DR TB patients for ADRs. The team ideally will consist of clinicians, pharmacists, nutritionists as well as the head nurse or matron of the facility. Detailed follow-up of suspected drug reactions would be used to define causality. The clinician who sees the patient reports any suspected ADRs to the PPB and National TB Program and contributes to public education on drug safety.

Pharmacy & Poisons Board (PPB)

The PPB will take responsibility for any regulatory action with respect to the implicated medicinal product/s. These actions will be officially communicated to the drug manufacturers, who have liability for the drug. The PPB will:

- Receive reports from health workers and other sources
- Develop and maintain ADR database
- Detect ADR signals and take necessary action on received reports
- Support the clinical review team to investigate relevant ADR reports
- Send ADR reports to Uppsala Monitoring Centre
- Provide feedback to the users on reported ADRs through quarterly newsletters
- Establish and provide secretariat for the Expert Safety Review Panel
- Advocacy, Training and Education
- Provide support to whole system
- Communication / IEC Implement appropriate.

Managing Adverse Effects of Anti-Tuberculous Drugs 1st line medicine

Table 15.2: Anti TB Drugs adverse effects

Adverse Effect	Drug(s) Probably Responsible	Management
Minor		**Continue anti-TB drugs, check drug doses**
Gastrointestinal (Nausea, vomiting, anorexia)	R, H, Z, RPT	Rule out other causes Conduct liver function tests to rule out drug-induced hepatic dysfunction Give drugs with small meals or just before bedtime and advise patient to swallow pills slowly with small sips of water. If symptoms persist or worsen, consider the side-effect to be major and refer to clinician urgently
(Joint Pain) Arthralgia	Z	Aspirin, non-steroidal anti-inflammatory drug or paracetamol
Mild itching rash	H, RPT	Treat with antihistamine Prednisone may be added at 40mg/day and tapered gradually as the rash clears A topical cream may be added
Peripheral neuropathy	H	Pyridoxine 100 - 200 mg daily
Orange/red urine, tears, etc.	R	Reassurance. Patients should be told when starting treatment that this is normal.
Major		**Stop responsible drug(s) and refer to clinician urgently**
(Flushing reaction) Skin rash with or without itching	E > Z > R > H	Reassure patients and inform about avoiding tyramine and histamine-containing foods (e.g. tuna, cheese red wine) while receiving Isoniazid If flushing is bothersome to the patient, an antihistamine may be administered to treat the reaction If persist, stop anti-TB drugs; give symptomatic treatment and wait for resolution of symptoms before rechallenge
Hepatitis	Z > H > R >RPT (R can also cause asymptomatic jaundice)	Stop anti-TB drugs, wait for resolution of symptoms and liver function tests before rechallenge
Visual impairment (optic neuritis)	E	Stop E and exclude other causes
Shock, purpura, acute renal failure	R	Stop R
Hypersensitivity	H, RPT	if severe reaction e.g. thrombocytopenia, hypotension, discontinue treatment until the reaction resolves. Refer to hospital

Recommended approaches to improving Pharmacovigilance

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
- 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

Table 15.3: Indicators to monitor in Pharmacovigilance

Indicator	Indicator definition	Frequency	Source of data
Frequency of ADRs associated with target treatment	**Numerator:** Number of ADRs attributed to target treatment among patient on aDSM **Denominator:** Number of TB cases included in aDSM during at a given period	Quarterly	TIBU/PPB

The proportion of MDR-TB and or RR patients with reported adverse drug event	**Numerator:** Number of MDR-TB cases with one or more serious adverse events. **Denominator:** Total number of MDR-TB cases reported in each period.	Quarterly	TIBU/PPB

ACTIVE DRUG SAFETY MONITORING AND MANAGEMENT (aDSM)

KEY HIGHLIGHTS

- aDSM complements the efforts and capacity of the existing pharmacovigilance systems present, to address gaps in safeguarding patient safety and help increase knowledge on treatment regimens.
- aDSM is an essential component on the management of both drug sensitive and drug resistant TB done in a patient centered care approach to achieve the most desired able therapeutic benefits based on benefit/risk analysis to the patient.

aDSM is defined as active and systematic clinical and laboratory assessment of patients while on treatment for XDR-TB, or with new TB drugs or novel MDR-TB regimens to detect, manage and report suspected or confirmed drug toxicities. The recording and reporting activities of aDSM primarily target the serious adverse events (SAEs) as a basic requirement. The appropriate and timely management of ADRs is an integral component of aDSM and patient care

aDSM components

1. Clinical monitoring
    - active and systematic clinical and laboratory assessment during treatment to detect drug toxicity and AE
2. Management of AEs in a timely manner (Access to ancillary drugs)
3. Systematic and standardized recording and reporting of AEs
    - Data collection to include safety data
    - SAEs and AEs of special interest to be reported to the Ppb and TB program for causality assessment
    - Regular meetings between TB program and regulatory authorities.

Levels of aDSM monitoring

There are three levels of aDSM monitoring that may be used in depending on the human resource capacity, namely:

1. Core package: requires monitoring and reporting of all SAEs

2. Intermediate package: includes SAEs and AEs of special interest

3. Advanced package: includes all AEs of clinical significance

ADR risk factors

- Advanced age
- Diabetes mellitus
- Malnutrition
- Anemia
- Pregnancy and lactating mothers
- other medications
- Alcoholism
- Liver failure
- Chronic renal failure
- HIV infection.

Table 15.4: Classification of the severity of the adverse side effects

Severity	Definition
Mild	The adverse event does not interfere in a significant manner with the patient's normal functioning.
Moderate	The adverse event produces some impairment in the patient's functioning but is not hazardous to the health of the patient.
Severe	The adverse event produces significant impairment or incapacitation of functioning.
Life-threatening	The adverse event causes extreme impairment of functioning, requiring hospitalization and if left untreated could result in the death of the patient.

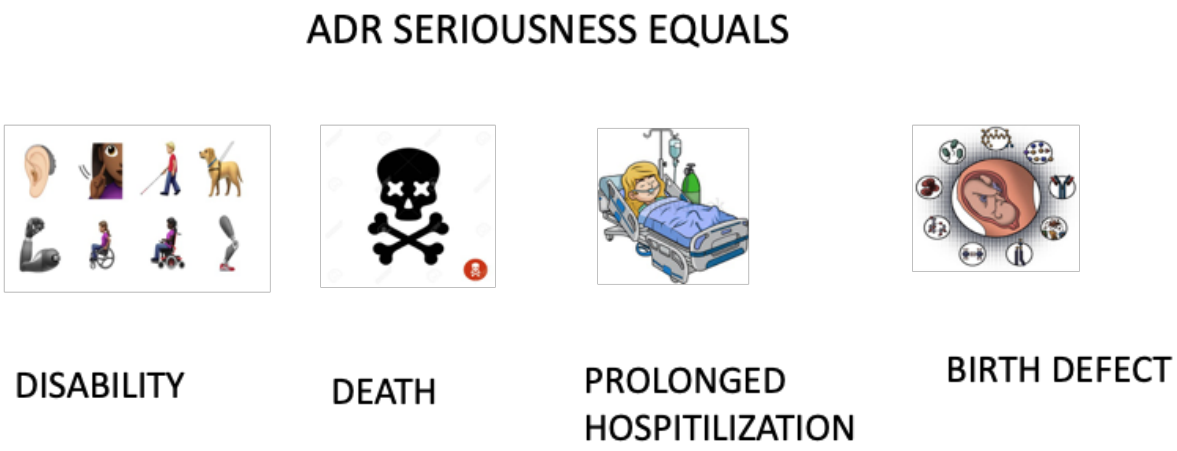
ADRs of clinical significance

ADRs of clinical significance includes Serious Adverse Drug Reaction (SADRs) defined as any untoward medical occurrence that is either (i) serious, (ii) of special interest, (iii) leads to discontinuation or change in the treatment or (iv) otherwise judged as clinically significant. It includes, at any dose:

- Results in death, hospitalization, significant disability/incapacity, life-threatening; congenital anomaly or a birth defect,
- AEs of interest in relation to seriousness, severity or causal relationship to the DRTB treatment, pertaining to the following medical conditions: Peripheral

neuropathy, Myelosuppression, Prolonged QTcF interval, Optic nerve disorder (optic neuritis), Hepatitis, Hearing impaired, Acute kidney injury, Hypokalemia and Hypothyroidism.

Figure 15.2: Serious adverse reactions



References: nbcnews.com; 123rf.com; friendlystock.com; connection,teratology.org

Detection of ADRs and Adverse events

ADRs and adverse events can affect both physiological and pathological pathways making them difficult to distinguish. The step-wise approach below is recommended for assessing ADRs;

a) Ensure the correct medication and dosing is prescribed to the patient

b) Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient;

c) Determine the time interval between the beginning of drug treatment and the onset of the event;

d) Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient's status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.

e) Analyse the alternative causes (other than the drug) that could on their own have caused the reaction

f) Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the National PV Centre which is PPB.

Principles of management

- Early identification and treat immediately & adequately
- Rule out other causes
- Consider additive or potentiating SE with concomitant therapy
- Consider drug-drug interaction
- For minor and moderate reactions: Symptomatic management (recommended algorithms, OTCs and ancillary medications)
- For moderately severe reactions: Reduce dosage/ frequency of the suspected drug.
- Severe reactions: Patient hospitalized and managed. If a reduced dose does not help to resolve stop and replace or immediate stoppage of all treatment or removal of a drug from the regimen.

Clinical grading and management of adverse reaction of DRTB treatments

1. Peripheral Neuropathy

Possible anti-TB drug that causes neuropathy: Cs, Lzd, H,

Table 15.5: Grading peripheral neuropathy

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life-threatening
Neurosensory alteration (including paraesthesia and painful neuropathy)	*Asymptomatic with sensory alteration on exam or minimal paraesthesia causing no or minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing greater than minimal interference with usual social and functional activities*	*Sensory alteration or paraesthesia causing inability to perform usual social and functional activities*	*Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions*
Action	Monitor. If symptoms improve after 2 weeks, consider restarting these drugs. **Consider restarting Lzd at a lower dose.**	Stop Cs and Lzd (high dose H). If symptoms resolve after 2 weeks, consider restarting Cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting Cycloserine. **Do not reintroduce Lzd.**	Stop Cs and Lzd. If symptoms improve after 2 weeks consider restarting Cycloserine. **Do not reintroduce Lzd.**

Symptomatic relief for peripheral neuropathy:

- ***Non-steroidal anti-inflammatory drugs*** or acetaminophen helps alleviate symptoms.
- ***Tricyclic antidepressants*** have also been used successfully. Start amitriptyline 25 mg at bedtime. The dose should be increased to a maximum of 150 mg daily for refractory symptoms.
- ***Carbamazepine*** is effective in relieving pain and other symptoms of peripheral neuropathy.

2. Myelosuppression

3. Possible anti-TB drug causes: Lzd, Cfz,

NOTE:

If possible, the co-administration of amitriptyline and Lzd should be avoided due to potential risk of serotonergic syndrome. Symptoms of serotonergic syndrome include high body temperature, agitation, increased reflexes, tremor, sweating, dilated pupils, and diarrhoea.

Table 15.6: Grading Myelosuppression

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Absolute neutrophil count	*1000 – 1300/ mm3*	*750 – 999/ mm³*	*500 – 749/mm³*	*< 500/ mm³*
Haemoglobin*[6]	*10.5 - 9.5 g/dL*	*9.4 - 8.0 g/dL*	*7.9 - 6.5 g/dL*	*< 6.5 g/dl*
Platelets decreased	*100.000-124.999/mm³*	*50.000-99.999/ mm³*	*25.000-49.000/mm³*	*<25.000/mm³*
WBC decreased	*2.000-2.500/ mm³*	*1.500-1.999/mm³*	*1.000-1.499/mm³*	*<1.000/mm³*
Action	Monitor carefully, and **consider reduction of dose of Lzd (300mg daily or 600 mg thrice weekly)**	Monitor carefully, and **consider reduction of dose of Lzd to 300mg daily**; In case of Grade 2 neutropenia, **stop Lzd immediately. Restart at reduced dose once toxicity has decreased to Grade 1.**	Stop Lzd immediately. **Restart at reduced dose once toxicity has decreased to Grade 1.**	Stop Lzd immediately. **Consider haemotransfusion or erythropoietin. Restart at reduced dose once toxicity has decreased to Grade 1.**

[5] Hemoglobin should be interoperated with baseline hemoglobin value

Prolonged QTcF Interval

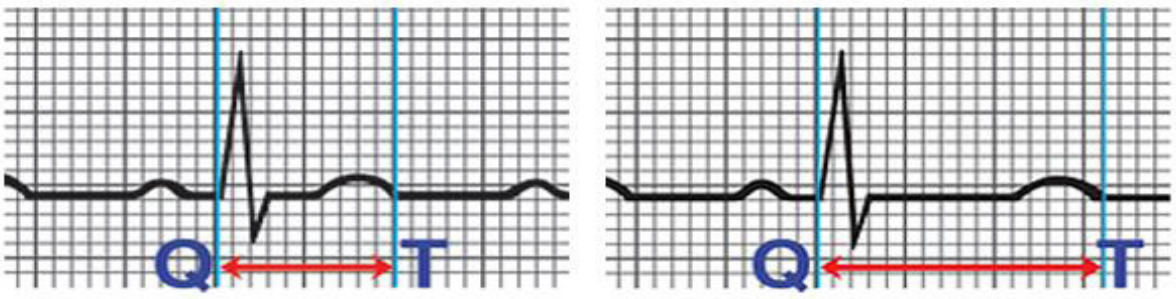
Possible anti-TB drug causes: Bdq, Mfx, Lfx, Cfz

Possible other causes:

- Many other drugs can cause QT prolongation; erythromycin, clarithromycin, quinidine, ketoconazole, fluconazole, antipsychotics haloperidol, chlorpromazine, risperidone, methadone and anti-nausea drugs that include ondansetron/ granisetron, domperidone,

  Genetic causes such as long QT syndrome; hypothyroidism.

Figure 15.3: Normal vs Prolonged Q-T intervals[6]



Note: *The QT interval is measured from the beginning of Q-wave to the end of the T wave. Its duration varies depending on the heart rate. Its measurement must be corrected according to the heart rate. It is recommended to use the Fredericia method to calculate the QTcF (Pharmacy.umaryland.edu)*

Table 15.7: QTcF Prolongation (ms) Gender cut-offs

QTc Prolongation (ms)	*Normal*	*Borderline*	*Abnormal*
Men	≤ 430	431- 450	>450
Women	≤ 450	451-470	>470

Table 15.8: Grading of prolonged QT interval

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life-threatening
Prolongation of QTcF	*Asymptomatic, QTcF 450 – 480 ms* *OR Increase interval **< 0.03** sec above baseline*	*Asymptomatic, QTcF 481 – 500 ms* *OR Increase in interval 0.03–0.05 sec above baseline*	*Asymptomatic, QTcF >= 501 ms without signs/ symptoms of serious arrhythmia* *OR Increase in interval ≥ 0.06 sec above baseline*	*QTcF >= 501ms or > 60 ms change from baseline and one of the following: Torsade de pointes or polymorphic ventricular tachycardia or signs/ symptoms of serious arrhythmia*
Action	Monitor more closely; **at least weekly ECG until QTcF has returned to grade 1 or less.**	Monitor more closely; **at least weekly ECG until QTcF has returned to grade 1 or less.**	**Stop the suspected causative drug.** Hospitalize and replete electrolytes as necessary.	**Stop the suspected causative drug**. Hospitalize and replete electrolytes as necessary.

Suggested Management strategy

1. **Checking and eplenishing serum electrolytes**

   - Serum potassium (K^+), ionized calcium (ionized Ca^{++}), and magnesium (Mg^{++}), should be obtained in the event a prolonged QT interval is detected.
   - The cause of abnormal electrolytes should be corrected
   - Whenever a low potassium is detected it should trigger urgent management with replacement and frequent repeat potassium testing (often daily or multiple times a day) to correct the levels of potassium.
   - If potassium is found low, always check magnesium and ionized calcium and compensate as needed. (If unable to check, consider oral empiric replacement doses of magnesium and calcium).

4. Optic Neuritis

Possible anti-TB drug causes: Lzd, E

Table 15.9: Grading of optic neuritis

	Grade 1 Mild	Grade 2 Moderate	Grade 3 severe	Grade 4 life-threatening
Visual changes (from baseline)	*Visual changes causing minimal or no interference with usual social and functional activities*	*Visual changes causing greater than minimal interference with usual social and functional activities*	*Visual changes causing inability to perform usual social and functional activities*	*Disabling visual loss*

Action	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**	**Stop LZD** immediately if there are any suspicion of optic neuritis. **Do not restart.**

Suggested management strategy

- Do not restart the suspected causative drug (Linezolid or Ethambutol)
- Refer patients to an ophthalmologist for further evaluation and management.
- Optic neuritis generally improves following cessation of offending drug, if it can be stopped early enough.

5. Hepatitis

Possible anti-TB drug causes: H, R, Z, Bdq,

Table 15.10: Grading of Hepatitis

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
ALT (SGPT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
AST (SGOT)	*1.25 – 2.5 x ULN*	*2.6 – 5.0 x ULN*	*5.1 – 10.0 x ULN*	*> 10.0 x ULN*
ACTION	**Continue treatment regimen**. Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Continue treatment regimen.** Patients should be followed until resolution (return to baseline) or stabilization of AST/ ALT elevation.	**Stop all drugs,** including anti-TB drugs; **measure LFTs weekly**. **Treatment may be reintroduced after toxicity is resolved.**	**Stop all drugs**, including anti-TB drugs; **measure LFTs weekly. Treatment may be reintroduced after toxicity is resolved.**

Suggested management strategy

Reintroduce anti-TB drugs once liver enzymes return to normal level. Anti-TB drugs should be reintroduced in a serial fashion by adding a new medicine every three to four days. The least hepatotoxic drugs while monitoring liver function tests after each new exposure.

Consider suspending the most likely offending drug permanently if it is not essential to the regimen. This is often the case for pyrazinamide if it is less likely to be effective by clinical history.

6. Hearing Impairment

Possible anti TB drugs causing hearing impairment: Km, Am, Cm.

Table 15.11: Grading Hearing impairment

	Grade 0: None	Grade1: Slight	Grade 2: Moderate	Grade 3: Severe	Grade 4: Profound
Decibel (dB) range	*25 dB or less*	*26-40 dB*	*Child- 31-60 *dB* *Adult- 41-60* dB*	*61-80 dB*	*>80 dB*
Severity	No/ Slight problems **Hears Whispers**	Hears/ repeats words in **normal voice** at 1 meter	Hears/ repeats words in **raised voice** at 1 meter	Hears words **shouted** into better ear	**cannot hear**/ understand shouted voice

**The grades/severity of hearing loss is also categorized differently for different age groups (see annex).*

Suggested management strategy:

Perform a monthly assessment of hearing loss and balance. Audiometry is helpful in detecting early high-frequency hearing loss that the patient may not even be aware of. If the patient is experiencing hearing loss, stop the injectable and replace it with a non-ototoxic drug. Even when non-ototoxic drugs are not available, stopping the injectable can be considered based on the patient's desire to maintain hearing. If moderate or severe vertigo, tinnitus (ringing in the ears) or vestibular disturbances arise, with or without significant hearing loss, consider decreasing frequency or stopping the injectable agent.

7. Acute Kidney Injury/Failure

Possible anti-TB drug causes: Aminoglycosides (Km, Am, Cm)

Table 15.12: Grading Acute kidney injury/Failure

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Acute Kidney Injury/ Chronic Kidney Disease	GFR= 60-89 mL/ min	GFR= 45-49 mL/ min	GFR= 30-44 mL/ min	GFR= 15-29 mL/ min and <15 mL/ min
Action	Consider **stopping injectable** until creatinine has returned to baseline. Consider **restarting the injectable at lower frequency** (e.g. MWF).	**Stop injectable** until creatinine has returned to baseline. Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**	**Stop injectable until creatinine has returned to baseline.** Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**	**Stop injectable until creatinine has returned to baseline.** Consider **restarting the injectable at lower frequency** OR **substitute** with a **non-nephrotoxic drug**

** The best measure of kidney function is Glomerular Filtration Rate (GFR).*

Suggested management strategy:

Monitor serum creatinine and electrolytes frequently in patients receiving injectable. Patients with pre-existing kidney disease, diabetes, or HIV are at high risk of injectable nephrotoxicity and may be monitored more frequently.

Repeat electrolytes if necessary:

Injectable nephrotoxicity may be associated with injectable-induced electrolyte wasting. For example, it is possible to see elevated creatinine and severe hypokalaemia/ hypomagnesemia at the same time. The aetiology of this phenomenon is unclear, but it may occur more often in HIV co-infected patients. Discontinue the suspected drug (usually the injectable). If the acute renal failure is severe, then stop all drugs. Follow serum creatinine and electrolytes closely until the creatinine has returned to baseline or has stabilized. Consider strict weight-based dosing of the injectable if the patient's weight is less than 50 kg. Suspend the injectable permanently if the nephrotoxicity recurs despite intermittent dosing, and add additional anti-TB drugs to reinforce the regimen.

9. Hypokalemia

Possible anti-TB drug causes: Cm, Km, Am

Table 15.13: Normal values of potassium level and quantity of KCL required

Potassium level Normal value (3.5-5.0 Meq/L)	Quantity of KCl
3.7 or more	None
3.4-3.6	40 meq
3.0-3.3	60 meq
2.7-2.9	80 meq
2.4-2.6	80 -120 meq
2.0-2.3	60 meq IV and 80 meq PO
<2.0	60 meq IV and 100 meq PO

Table 15.14: Grading Hypokalaemia

	Grade 1: Mild	Grade 2: Moderate	Grade 3: Severe	Grade 4: Life threatening
Hypokalaemia	3.4 - 3.0mmol/L	2.9 – 2.5 mmol/L	2.4 - 2.0 mmol/L or intensive replacement therapy or hospitalization required	< 2.0 mmol/L or abnormal potassium with paresis, ileus or life-threatening arrhythmia

Action	**Continue injectable.** **Start oral potassium replacement therapy**. **Check serum magnesium and replace if necessary**	**Continue injectable**. **Start aggressive oral potassium replacement therapy.** **Replace magnesium as necessary**.	**Consider stopping the injectable temporarily**. **Start IV potassium replacement therapy in addition to oral**. **Replace magnesium and other electrolytes as necessary**.	**Stop injectable** temporarily. **Start IV potassium replacement therapy** in addition to oral. **Replace magnesium** and other electrolytes as necessary.

Table 15.15: Side Effects Related to TB Drugs and Food Intake Recommendations

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 B6 Supplement daily	Alcohol	Hepatotoxicity, Cutaneous, hypersensitivity, Peripheral Neuropathy
Ethambutol	To be taken with food A	Avoid alcohol	Arthralgia, Retro bulbar neuritis.
Pyrazinamide	May be taken with food		Hepatotoxicity, Arthralgia, Nausea, Vomiting
Ofloxacin	Take with or after meals (Supplement with Vit B6)	Alcohol	Abdominal discomforts, nausea
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
Paraaminosalicylic acid (PAS)	Take with or immediately after food. Increase fluid intake	Alcohol	Gastrointestinal reactions Dizziness, Headache, Depression, Memory loss
Cycloserine	Supplement with vitamin B6	Alcohol	Dizziness, Headache, Depression, Memory loss
Prothionamide	Take with or after meals (Supplement with Vit.	Avoid Alcohol	Abdominal Discomfort, Nausea, Vomiting

Bedaquline	Take with or after meals (Supplement with Vit B6).	Avoid Alcohol	Prolonged QT, Hepatotoxicity, Nausea, vomiting, arthralgia, headache, itchiness,
Linezolid	Avoid foods rich in tyramine (fermented meat product, pickles)	avoid alcohol	Myelosuppression, Lactic acidosis, optic and peripheral neuropathy, skin reaction
Delanamide	Absorption increased after a standard meal		Serious Heart rhythm changes Nausea, Vomiting, Dizziness, Insomnia, Upper abdominal pain Anxiety, paraesthesia

Selected Serious Drug Interactions

Drug to drug interactions (DDIs) has recently received concern and increasingly reported attention. With new interventions, large number of drugs are manufactured and introduced into the market space every year, new interactions between medications needs to be monitored and reported. Some common drugs have specific drug-drug interactions that may require dose adjustment or substitution of the ARV or the other interacting drugs

Table 15.16: An overview of selected serious drug interactions

Antiretroviral	Bedaquline	Delanamide	Rifapentine
Efavirenz	Do not co-administer-Reduces BDQ by 50%	No interaction	No interaction
Nevirapine	No dose adjustment. No dose adjustment	Not expected	Interacts
Rilpivirine	Not expected	Not expected	N/A
Lopinavir/Ritonavir	Increase BDQ exposure: may lead to toxicity?	Increase DLM exposure: clinical relevance	Interacts
Atazanavir/ritonavir/ Raltegravir & Dolutegravir Darunavir/ritonavir	No interaction expected	Not studied, no interaction expected	Interacts with all except Dolutegravir
Raltegravir Dolutegravir	No interaction expected	Not studied, no interaction expected	No interaction

COMMODITY MANAGEMENT

16

The rational use of medicines, pharmaceutical and non-pharmaceutical including nutrition commodities, 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.

Commodity management is a key component of rational drug use. It is the process of developing a systematic approach to the entire usage cycle for a group of items. It is used in ensuring that the Right product, of the Right quality, in Right quantities is delivered at the Right time, at the Right place, to the Right customer.

Figure 16.1: Commodity logistics

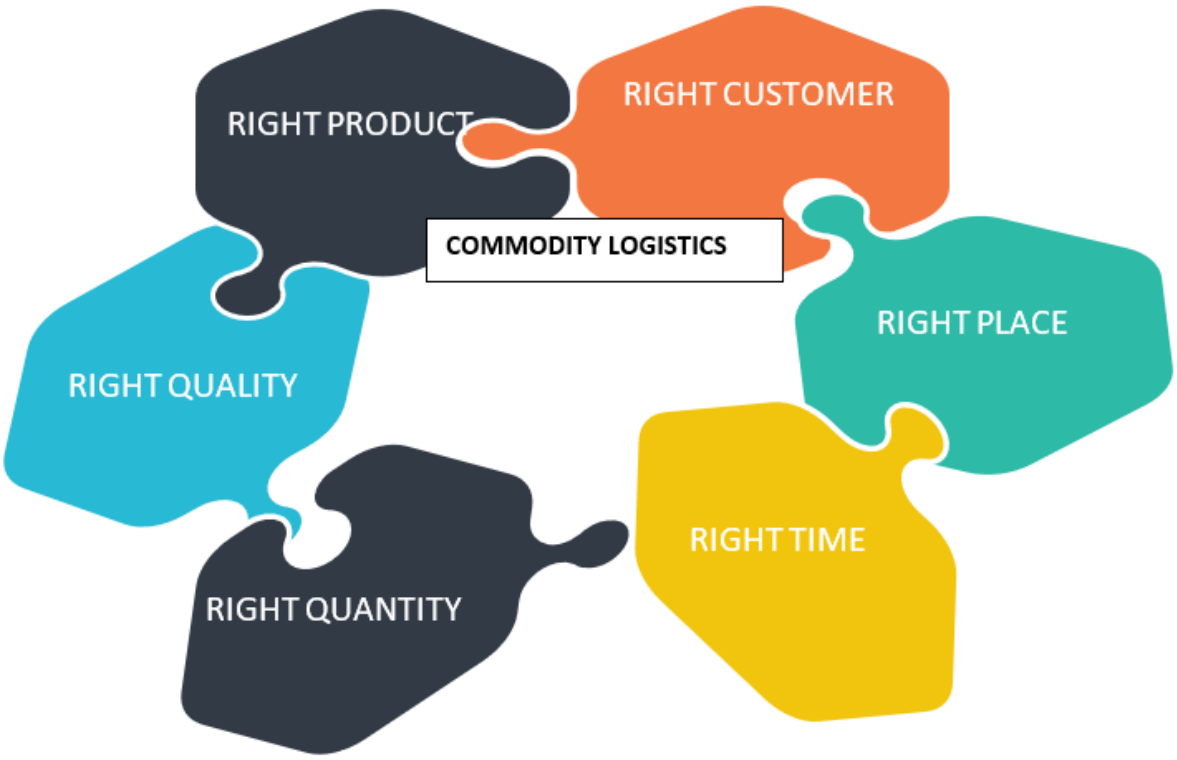
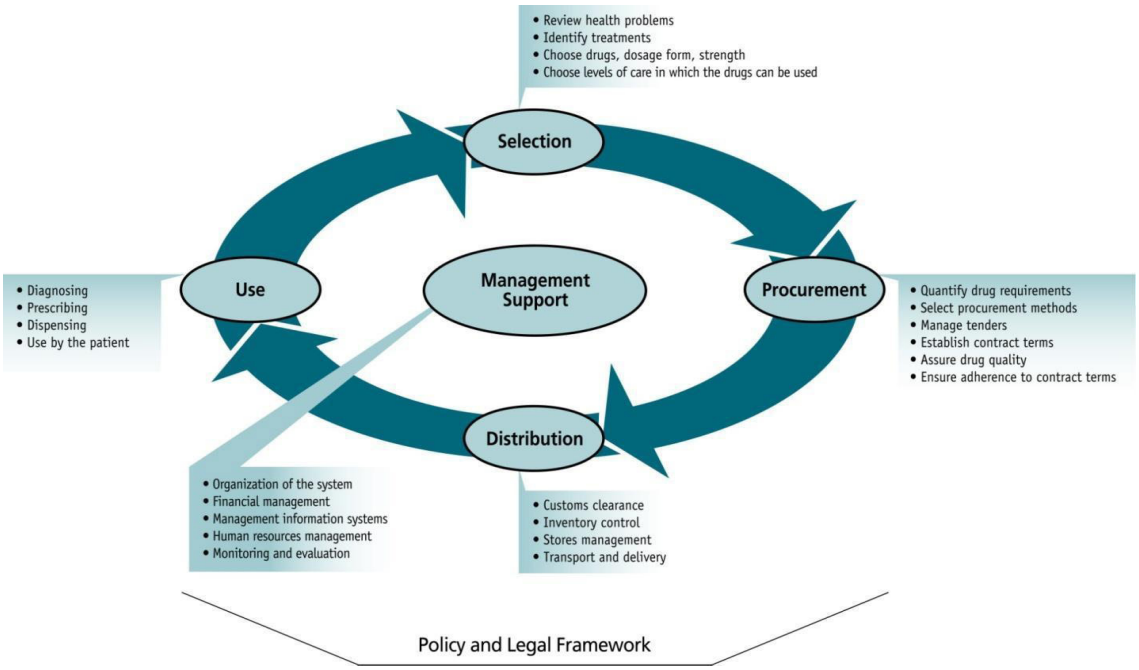


Figure 16.2: Commodity management cycle



16.1 Forecasting and Quantification

This is the process of estimating the quantities of medicines and other commodities including nutritional support that is required for a specific period of time in order to ensure uninterrupted supply of commodities. Accurate forecasting and quantification guarantees commodity security that alleviates shortages and stock-outs affecting service delivery. Quantification methods include consumption based and morbidity-based method.

16.2 Quantification methods used in TB commodities

16.2.1 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

16.2.2 Morbidity method

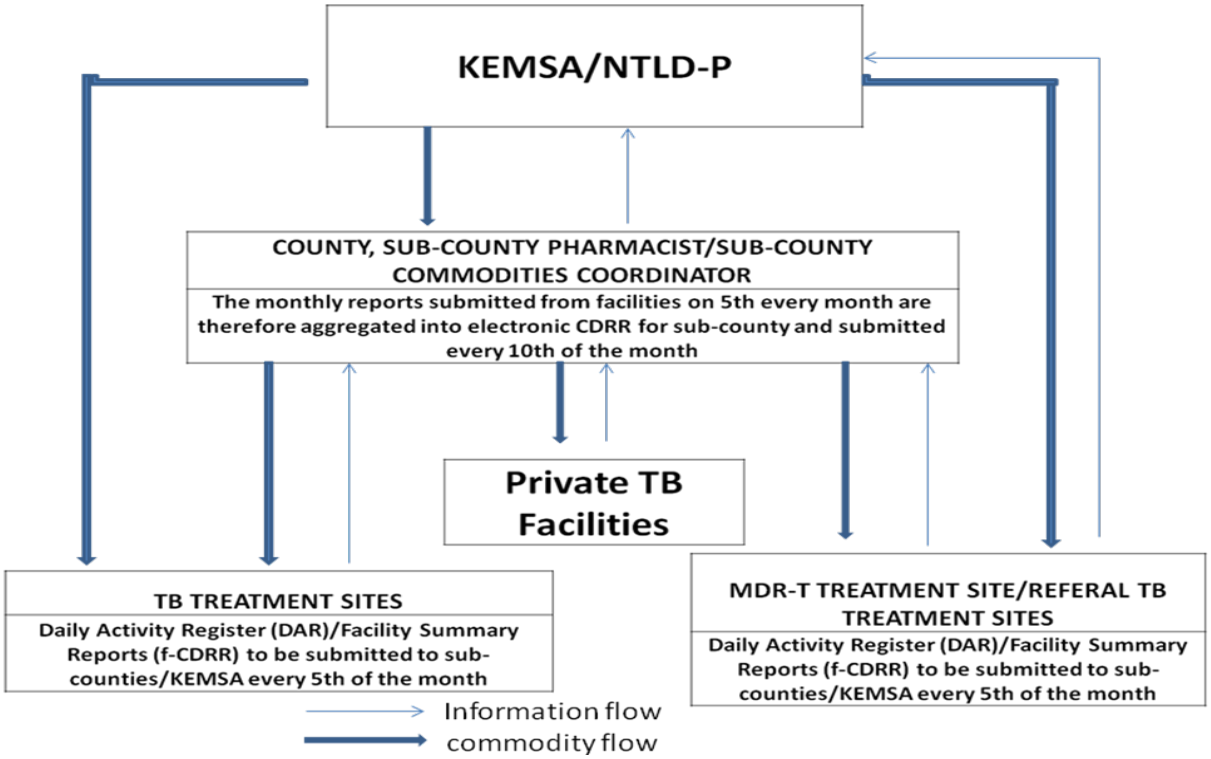
The morbidity-based method uses data about diseases and the frequency of their occurrence in the population (incidence or prevalence) or the frequency of their presentation for treatment.

This method forecasts the quantity of drugs needed for the treatment of specific diseases, based on projections of the incidence of those diseases.

16.2.3 Flow of Logistics

TB commodities are ordered anytime for DRTB patients with drugs delivered in 48hours by courier. The Facility consumption data report and request (FCDRR) tool is used for commodity reporting and requesting. Please refer to flowchart below

Figure 16.3: shows the logistic management information and commodity flow.



16.3 Reasons for accounting for TB commodities

It is essential for all TB commodities to be utilized prudently as effective management of commodities enables;

- Accurately determination of needs
- Prevention of stock outs
- Prevention of expiries
- Minimization of wastage
- Prevention of pilferage
- Sustainable funding

16.4 Stock keeping records

- Delivery Notes- A document that accompanies a shipment of goods, and provides a list of the products and their quantities
- Bin cards – This is store's record card of quantities of a particular commodity that records the quantities received, issued and balances the stocks of the commodity.
- S11/S12 – S11 is a form used to order a commodity from the store to pharmacy or dispensing room. S12 is a form used to order a commodity from the warehouse to the health facility store.
- Daily activity registers e.g. AL register and Tally sheets -
- SORF, Health facility monthly summaries-

16.5 Patient pack and supply box management

- **Patient Pack**

  A patient pack is the one every newly diagnosed DS-TB adult patient is allocated. This pack contains the drugs the patient will use for the entire duration of TB treatment. This pack should be titrated to ensure that it has the correct amount of drugs that is equal to the duration that the patient will be on treatment. The titration is done based on the **patient weight at diagnosis and during the course of treatment.** If there are excess drugs following titration, these should be put into the supply box. If there is a deficit in the patient pack following titration, the short fall is picked from the supply box. The adult patient pack contains 168 tablets of RHZE and 336 tablets of RH.

- **Supply Box**

  The supply box is the one that contains TB drugs that are either an excess from the patient pack or to be used to fill the deficit in the patient pack. The supply box can be used to provide drugs for patients on transit or to create a patient pack in-case of drug shortages.

  For purposes of tracking, one has to input the figures of drugs coming into and leaving the supply box in the DAR for TB drugs.

PATIENT SUPPORT, HUMAN RIGHTS AND SOCIAL PROTECTION

17

17.1 Introduction

The WHO End TB Strategy sets the required interventions to end the global TB epidemic by 2035. Pillar one of the strategy adopts a patient-centered approach that recognizes the individual who is sick as the direct beneficiary of TB care and strategies must be designed with this individual's rights and welfare in mind. The strategy, under Pillar 2 on Bold policies and supportive systems, places emphasis on ending TB through addressing social determinants of TB, including poverty alleviation policies and social protection programs and putting Universal Health Coverage policies in place. The National Strategic Plan for TB, Leprosy and Lung Disease (2019-2023) advocates for a more patient-centred focus. Patient support includes support from community and family members, health care workers and from the health care system through information, referral linkages, supplies of patient commodities (nutritional commodities, medicines and equipment).

1. **Universal Health Coverage in TB, Leprosy and Lung Health**
2. **Social protection through universal health coverage, nutrition and human rights**
3. **Key social support recommendations**
4. **Human Rights and TB, Leprosy and lung disease**
   a. A rights-based approach to TB
   b. Gender related barriers to TB services
   c. The Constitution of Kenya and protection of human rights
   d. Human Rights and Unequal Access to TB Care and Treatment
   e. Criminalization of TB Status: Involuntary Treatment, Isolation, Detention and Incarceration
   f. Patients' charter for tuberculosis care
   g. Guiding principles for implementing TB control activities at the workplace.

17.2 Universal Health Coverage in TB, Leprosy & Lung Health

Universal Health Coverage (UHC) is defined as ensuring that all people have access to the needed health services of sufficient quality while also ensuring that the use of these services does not expose them to financial hardships. The Government of Kenya is committed to attaining UHC by 2021 through expansion of the population covered with essential health services, strengthening and broadening the primary health care system, increasing health resource base and leveraging on information technology.

Together with other United Nations member states, Kenya is working toward worldwide universal health coverage by the year 2030.

KEY HIGHLIGHTS:

- **Universal Health Coverage has been piloted in 4 counties; Isiolo, Kisumu, Nyeri and Machakos.**
- **The Government of Kenya is committed to attaining UHC by 2021 through expansion of the population covered with essential health services, strengthening and broadening the primary health care system, increasing health resource base and leveraging on information technology.**
- **A survey conducted by the National TB program in 2017 found that 26.5% of TB affected households, including 86.4% of DR-TB affected households experienced catastrophic cost.**

17.2.1 Strategies towards Implementing UHC

1. Strengthening health systems in Kenya: Pooling of funds from NHIF in order to spread the financial risks of illness across a population.
2. Availability, accessibility and capacity building of health workers to deliver quality people-centered integrated care.
3. Investing in primary health care which has been known to be the most cost effective way to accessing essential healthcare.
4. Good governance, sound systems of procurement and supply of medicines, health technologies, well-functioning health information systems and other critical elements.

The health sector has identified the following UHC objectives:

1. Progressively increase the number of Kenyans accessing essential health services
2. Progressively expand the scope of the health benefit package that will be accessible to all Kenyans

3. Increase the number of Kenyans covered under prepaid mechanisms (such as health insurance, subsidies, direct government funding) to access health services
4. Increase the availability of quality essential interventions
5. Protect Kenyans from catastrophic health expenditures, and in particular the poor and vulnerable groups
6. Enhance equity and efficiency in allocating and using resources
7. Provision and maintenance of adequate health resources that will be appropriate for the delivery of health services
8. Strengthen leadership and governance within the health sector

17.2.2 UHC and primary health care

Primary health care is an approach to health and wellbeing centered on the needs and circumstances of individuals, families and communities. It addresses comprehensive and interrelated physical, mental and social health and wellbeing. Primary health care is the most efficient and cost effective way to achieve universal health coverage around the world.

17.2.2.1 Key components to address at primary health care delivery level:

i) Ensuring TB, Leprosy and other lung disease patients' *health problems are addressed through comprehensive promotive, protective, preventive, curative, rehabilitative, and palliative* care throughout the life course, strategically prioritizing key system functions aimed at individuals and families and the population as the central elements of integrated service delivery across all levels of care;

ii) *Systematically addressing the broader determinants of health* (including social, economic, environmental, as well as people's characteristics and behaviours) through evidence-informed public policies and actions across all sectors; and

iii) *Empowering individuals, families, and communities* to optimize their health, as advocates for policies that promote and protect the health and wellbeing, as co-developers of health and social services through their participation, and as self-carers and care-givers to others.

17.2.3 Role of counties in UHC

17.2.3.1 Planning for UHC

1. Ensure TB, leprosy and lung health are prioritized in the county integrated development plan as part of county health systems strengthening to align to UHC.
2. Develop roadmaps and annual work plans which incorporate TB, leprosy and lung disease for UHC implementation for their respective counties. This should take

into account the planning horizon with regards to human resources and physical infrastructure.

3. Put in place well defined quarterly implementation plan for TB, leprosy and lung disease.
4. Plan for and carry out annual and quarterly TB, leprosy and lung disease quarterly review meetings and Rapid Response Initiative (RRI) reviews.
5. Develop learning platforms through collecting data and information on TB, leprosy and lung disease for assessing the changes and impacts from the implementation.
6. Review and strengthen the county referral systems for the TB, leprosy and Lung disease program to reduce influx to the higher-level facilities.
7. Put in place a clear guide and enforce the gatekeeping mechanism on TB, leprosy and lung disease patients' rights on referral processes to avoid high influx in Level 4 facilities as per the referral strategy.
8. Set up M&E units for TB, leprosy and lung disease within the Counties; put in place strong expertise on M&E for the implementation of plans, for example through RRIs, as well as collecting data/information for assessing the changes and impacts from the implementation.

17.2.3.2 Communication for UHC

1. Create public awareness on the importance of taking care of one's health especially on patients who have developed signs and symptoms for TB, leprosy and lung disease.
2. Create public demand to access quality and affordable TB, leprosy and lung health services.
3. Create public awareness on their right to health and the responsibility for their own health including the importance of paying for national health insurance.
4. Develop SOPs on and train health sector officials and health providers on how to respond to public and media concerns and/or allegations. Public communication at the time of crisis should be done in a timely and transparent manner with empathy.
5. Improve communication skills while providing TB, leprosy and lung disease services
6. Communicate with all actors in a manner that they understand their rights, responsibilities and opportunities to maximize the benefits of UHC.
7. Strengthen public understanding of and demand for UHC by communicating what achieving this goal would mean for individuals and communities; create opportunities for citizens and communities to hold their leaders accountable.
8. Set up a structured system for TB, leprosy and lung disease patients channeling their complaints, and receiving feedback on time.

9. Provide learning initiatives such as training and exchange visits to help counties bridge communications gaps and reinforce UHC reform objectives.
10. Initiate messages and communicate through: billboards; radio; stories and information on mass media (radio, newspaper, TV, etc.); and pamphlets for mass distribution.

17.2.3.3 Expansion of the population covered by prepaid mechanisms (subsidies, direct funding, insurance)

1. Provide TB and leprosy services at no cost to all the populations in L1 to L5 with a view to ensuring financial protection.
2. Strengthen advocacy, communication and social mobilization on the uptake of health insurance for TB, leprosy and lung health services.
3. Encourage enrolment of households into a health insurance scheme with focus on offering subsidies to the poor and the vulnerable.
4. Institutionalize the biannual household registration including social mapping by CHVs as prescribed in the Community Health Strategy.
5. Implement a standard incentive package for CHVs

17.2.3.4 Monitoring and evaluation

1. Collect and report TB, leprosy and lung disease statistics on DHIS and other national reporting platforms
2. Regularly update county-specific dashboards to show progress
3. Document and share best practices in TB, leprosy and lung disease for mutual learning and replication
4. Continuously assess readiness and monitor improvement in preparedness to deliver TB, leprosy and lung health services.

17.3 Social Protection

17.3.1 Background

The International Labor Organization 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:

- General poverty and social exclusion
- Lack of affordable access to health care
- Lack of labor market protections
- Lack of work-related income.

KEY HIGHLIGHTS:

- **Social protection is a set of interventions whose objective is to reduce social and economic risk and vulnerability, and to alleviate extreme poverty and deprivation.**
- **Social protection consists of policies and programs designed to reduce poverty and vulnerability by promoting efficient labour markets, diminishing people's exposure to risks, and enhancing their capacity to manage economic and social risks, such as unemployment, exclusion, sickness, disability and old age.**
- **A survey conducted by the National TB program in 2017 found that 26.5% of TB affected households, including 86.4% of DR-TB affected households experienced catastrophic cost**

In 2017, Kenya's Division of National TB Leprosy and Lung disease Program (DNTLD-P) conducted a nationally-representative, health-facility based survey to assess the magnitude and main drivers of costs incurred by TB patients in Kenya. The survey found that 26.5% of TB affected households, including 86.4% of DR-TB affected households, experienced catastrophic costs. The median total cost borne by patients seeking diagnosis and treatment per TB episode was Kshs 26,041.49. Median total cost of Kshs 25,874.00 and Kshs 145,109.53 was incurred as a result of an episode DS-TB and DR-TB respectively. Direct non- medical costs due to nutrition and food supplements accounted for 68.5% of expenses (Ksh 17,739.71).

These costs have been identified as barriers to accessing the full scope of TB services. To get by, 27.8% of TB patients used negative coping mechanisms like taking a loan, use of savings and sale of assets to meet the expenses. This financial hardship resulting from direct and indirect costs when accessing health care for TB may adversely affect living standards and the capacity of households to pay for basic needs. Further, the Kenya TB Patient Costs Survey, demonstrated the negative consequences faced by TB patients including 63 percent lost jobs, nine percent of the household's children disrupted school and 36 percent faced social exclusion. These negative consequences make TB patients less likely to present for care, complete testing, initiate and adhere to treatment, leading to increased transmission of the disease, morbidity and mortality.

With the findings, the DNTLD-P developed a 'Kenya Social Protection Policy for Tuberculosis and Leprosy Patients 2018'. The overall goal of the policy is to "Reduce the proportion of affected families who face catastrophic costs due to TB and leprosy" The policy recognizes that social protection needs to be an integral part of TB and leprosy prevention and care to achieve this target. It also proposes a comprehensive integrated social protection floor for people with TB and Leprosy that includes: cash transfers, food assistance, health insurance and advocacy of social security legal frameworks that cover both formal and informal workers.

The Ministry of Health through DNTLD-P, began enrolling all DR-TB patients to the National Hospital Insurance Fund (NHIF) scheme in 2017. A total of 310 newly diagnosed DR-TB patients, including mono resistant TB patients, benefitted from NHIF social

support in 2019. Additionally, 766 DOT supporters were supported to offer community DOT while 1,160 patients received monthly cash transfers of Ksh. 6,000 in the same year.

17.3.2 Social protection through universal health coverage, nutrition and human rights

TB treatment is inextricably involved in a host of psychological, social, and economic problems, these guidelines were developed to help providers establish and enhance social support services in a TB clinic. The purpose of the guidelines is to help the worker establish social services, develop a therapeutic alliance with clients, create an intake form to identify barriers to TB, leprosy and lung disease treatment and formulate goals to reduce those barriers and to increase client functioning, counsel and help clients achieve their goals, form support groups, and lead or participate in case management.

Patient support under UHC, nutrition, gender and human rights are therefore aspects that are cross cutting to ensure a comprehensive approach in the delivery of TB, leprosy and lung health interventions. The approach should ensure efficiencies and effectiveness in health programming. It therefore demands and calls for a multidisciplinary and multi-sectoral collaboration in implementing the interventions.

Social protection for TB and leprosy patients is one way of demystifying the common belief that these diseases are "poverty disease". It plays a major role in restoring dignity of individuals, households and communities and alleviates poverty, vulnerability and social exclusion for both TB patients and their households.

17.3.2.1 Social Protection: What should a health care worker do?

All TB, leprosy and lung disease patients should be eligible for UHC, Social protection, nutrition, gender and human rights services. In providing appropriate services, consider eligibility criteria for the patients to be enrolled for the available support.

Psychosocial support - ongoing counselling for patients (*refer to Chapter 18: Advocacy and Communication for detailed guideline)* and households, identification and reporting of adverse drug effects, TB treatment literacy, Monitoring and reporting of TB human rights violations

Mental health - assess patients' wellbeing and refer for psychological support, link to social support groups/ structures in the community for adherence counselling, Assess harmful alcohol and drug use and link for appropriate rehabilitation.

Table 171: Key Social Support recommendations of the Guidelines

Patient needs identification	Refer to social protection support based on identification criteria existing	Link patient to social support services
Nutrition Support	Refer to existing nutritional support system: • Supplementary (For Moderate Acute Malnutrition) • Therapeutic feeding (For Severe Acute Malnutrition) • Food insecurity support (For Households with food insecurity)	Link for Supplementary/ therapeutic support at facility level • Link and refer for food security & sustenance community systems/ programs e.g. Income Generating Activities, Food basket • Follow up patients for progress and advise accordingly in every facility visit or review
Patient psycho-Social well being	Psychological support -: Assess patient for Mental health status *(use appropriate tools)* • Adherence support for patient and family • Evaluate for Adverse drug reactions (Psychosis) • Assess and follow up on Patient/family treatment literacy	• Refer to appropriate support groups & DOTS support • Consider differentiated care for patient • Refer for expert advice and follow up through a multidisciplinary team (MDT) • Link to patient/family support group • Follow up patients for progress and advise accordingly in every facility visit or review
Patient psycho-Social well being	Social Support: Assess patient for social challenges • Harmful drug use and alcohol abuse • Access to social utilities e.g. proper sanitation such as clean water, proper housing, etc. • Cultural and religious factors	• Refer and link for rehabilitation services ensure patient consent and sign on patient consent form • Link to appropriate patient support groups • Engage different stakeholders (Multi-sectoral approach) • Support counselling to patient and caregiver/family • Follow up patients for progress and advise accordingly in every facility visit or review

Patient support for Cost of access to health services	• Medical cover for appropriate health services • Cash transfers • Patient benefit package e.g. Waiver, UHC, etc.	• Advise on individual patient contributions to health insurances or medical schemes for medical services especially for DS TB, leprosy and lung health services • Immediate linkage of DR TB patients, or caregiver in the case of a minor, to the Sub County/County level TB Coordinators for enrollment in the cash transfer program • Link patient to UHC benefit package where available • Follow up patients for progress and advice accordingly in every facility visit or review
Assess for human rights & gender issues	• Address family support for patient's wellbeing • Address gender related challenges • Address Stigma and discrimination related circumstances, e.g. loss of opportunities - job, school, community and health services • Supply and access to appropriate commodities for the highest attainable standards of health (accessible, acceptable, affordable and of good quality) • Consider rights of Health care worker	• Sensitize patient and family on patient charter and facility service charter • Refer for differentiated care on gender related interventions • Consider MDT approach such as expert groups which include Patients e.g. TB, Leprosy, Lung health Champions • Ensure confidentiality and service delivery in dignity for patients • In cases of human rights violations, link to available pro bono services for legal advice e.g. KELIN, CREW, HIV and AIDS tribunal, FIDA, etc. • Refer to the SOPs on Gender & Human rights • Meaningfully engage stakeholders (TB Champions and advocates, CHMTs) in ensuring efficiencies in commodity supply at all levels of healthcare cascade for advocacy purposes • Educate and sensitize HCWs on their rights, roles & responsibilities in TB and related diseases • Follow up patient for progress and advise accordingly in subsequent facility visit/ reviews

Reference material: *https://www.google.com/url?q=https://www.who.int/genomics/public/patientsupport/en/&sa=D&ust=1581489211589000&usg=AFQjCNF9BQsjfDtgbp6ZVz4j56uPXHN8Uw*

Source: *Utafiti Sera on Social Protection (2016)*

17.4 Human Rights and TB, Leprosy & Lung Disease

17.4.1 Background

Kenya is listed among the 30 high burden countries with a triple burden of TB, TB/HIV and MDR-TB. Due to the infectious nature of TB, measures to prevent, manage, and treat the disease have led to undesirable violations of human rights of TB patients. A good example was the practice of arrest and detention in prisons of persons suspected of having defaulted on their TB medication in Kenya. This necessitates the need for advocacy to integrate a human rights based approach to TB prevention, management, and treatment.

17.4.1.1 The Constitution of Kenya and protection of human rights

The Constitution of Kenya (CoK) has an expansive and progressive Bill of Rights that sets the stage for the promotion and protection of the rights of all persons, including persons with TB. Article 19 (1) provides that the Bill of Rights is an integral part of Kenya's democratic state and is the framework for social, economic and cultural policies. Article 10 of the CoK is particularly important to the TB response as it provides guidance in relation to formulation and implementation of laws, policies, and strategies on TB prevention and management. TB strategies in Kenya must be formulated and implemented in a manner that respects the national values, especially through ensuring the participation of TB affected communities. The most prominent provision of the CoK in the TB response is Article 43 that guarantees the right to the highest attainable standard of health. The State is under an obligation to take legislative, policy and other measures, including the setting of standards, to achieve the progressive realization of the right to health. By virtue of Article 2 (6) of the CoK, international instruments that Kenya has ratified form part of the Laws of Kenya. These international instruments provide a sound framework and basis for holding the government accountable where gaps exist at the domestic level.

The Health Act 2017 prescribes the right to health as:

i) Progressive access for provision of promotive, preventive, curative, palliative and rehabilitative services;

ii) Right to be treated with dignity, respect and have their privacy respected;

iii) Right to informed consent;

iv) Right to privacy and confidentiality, among others.

The local government and leadership should ensure inclusion of and involvement of TB champions and TB communities which is crucial to achieve better TB control outcomes. The TB community is key in holding duty bearers accountable in provision of quality TB and healthcare services. This also empowers the community to monitor service delivery, take part in decision making processes and platforms in the community on matters health and development and support in addressing wider social determinants of TB in an integrated manner.

Article 21 (3) provides: All State organs and all public officers have the duty to address the needs of vulnerable groups within society, including women, older members of society, persons with disabilities, children, youth, members of minority or marginalized communities, and members of particular ethnic, religious or cultural communities.

Health providers on the other hand have, among other rights, the right to a safe working environment that minimizes the risk of disease transmission. This is important in the protection of HCWs in the TB response.

17.4.1.2 Key principles of human rights

Equality and Non-Discrimination: This principle emphasizes that one should not be treated differently on grounds of race, sex, pregnancy, marital status, health status, ethnic or social origin, colour, age, disability, religion, conscience, belief, culture, dress, language or birth.

Universality of Rights: This principle focuses on the dignity of all human beings and assumes that all human beings, irrespective of their circumstances or environments have a right to equally enjoy all human rights.

Human Rights are Indivisible: This principle emphasizes the equal importance of all human rights. It avoids the temptation to classify human rights into categories of important and not important.

Human rights are interrelated: This principle emphasizes that the fulfillment of one's right often depends, wholly or in part, upon the fulfillment of others. Example: Fulfillment of the right to health may depend, in certain circumstances, on fulfillment of the right to clean water & food, development, to education or to information.

Participation and Inclusion: All people have the right to participate in and access information relating to the decision-making processes that affect their lives and well-being. Rights-based approaches require a high degree of participation by communities, civil society, minorities, women, young people, indigenous peoples and other identified groups.

17.4.1.3 Actors in the Human Rights field

Right or claim holder: The person who enjoys the human right and can claim for it. A **valid claim r**efers to the human right that can be enjoyed.

Duty bearer: A person or institution that is responsible to ensure that an individual obtains his rights. In most cases the government is the ultimate duty bearer. But there may be other duty bearers such as private actors and individuals. **Correlative duty** refers to what the duty bearer must do in order to ensure that citizens obtain the rights.

17.4.1.4 A rights-based approach to TB

Human Rights-based violations and the failure to fulfill human rights obligations increase individuals' vulnerability to contracting TB and reduce access to diagnostic, prevention and treatment services. People affected by TB usually suffer a double burden: the impact of the disease as well as the consequential loss of other rights. For key populations, due to additional stigmatization, the burden is in fact triple.

KEY HIGHLIGHTS:

- **A human rights-based approach to TB articulates the rights of people living with and vulnerable to TB, including the rights to life, health, non-discrimination, privacy, informed consent, housing, food and water.**
- **The approach focuses on the social and economic determinants of the disease.**
- **It articulates the domestic and international legal obligations of governments and non-state actors to ensure quality testing and treatment for TB is available and accessible without discrimination.**
- **The approach aims to create an enabling legal environment for the research and development of new tools for managing TB.**

A rights-based approach to TB is founded on respect for the dignity and autonomy of people affected by TB. It articulates and protects individual freedoms and entitlements, and is built on governments' obligations to respect, protect and fulfill the right to health. The approach focuses on the underlying determinants of TB through the lens of social, economic and cultural rights.

A human rights-based approach to TB also has components related specifically to the collection and use of data on TB key populations. Most importantly, the rights to privacy and confidentiality of all members of key populations must be explicitly acknowledged and protected during the collection and use of data. This is required under human rights law and necessary to ensure effective and sustainable interventions. In addition, countries must involve key populations in the design, implementation and evaluation of data collection and use efforts.

A rights-based approach requires that special attention be paid to the needs of groups most vulnerable to TB in the design and implementation of health policies, including the poor, people living with HIV, prisoners, migrants, women, children, and people who use drugs. The approach also encourages and facilitates the active and informed participation of affected individuals and communities in decision-making processes affecting their health. A rights-based approach has been applied successfully to HIV prevention and treatment throughout the world. The mobilization of affected communities in grassroots campaigns has spurred research and development of new medicines and lowered the prices of existing drugs. People living with HIV have claimed their rights to information in a simplified language, participation, and informed consent, and won greater protections against discrimination through litigation and advocacy based on constitutionally derived human rights.

17.4.1.5 Gender related barriers to TB services

Tuberculosis affects men and women differently, epidemiologically, biologically and socially. In order to eliminate TB, a TB response team must address the gender-related barriers to accessing TB services and include key and vulnerable populations. Females

are more likely to seek health care earlier and more frequently than males. However, females face socio-economic barriers to accessing health services since they are usually not as economically empowered as men. As a result of financial disadvantage, some women have to request permission from their husbands so as to seek health services. Money and power are barriers to health services for women. There is pressure for males to be seen as strong and macho and this may hinder them from seeking health services for TB, Leprosy or lung disease symptoms. Additionally, the labor task force in Kenya is largely informal and getting time off work to go to a health facility is challenging for casual laborers who are usually paid per day; this is a barrier to accessing health services during work hours (8 am to 5 pm) and also violates the rights of the casual workers. Majority of the casual laborers in the construction industry, factories and privately owned public transportation systems are males. The lack of freedom to have permission from casual labor employers for sufficient time to seek health services without losing the daily income is a major contributor to poor health seeking behavior in males in Nairobi. Additionally, TB services are usually only offered in the morning.

A study conducted by KELIN Kenya, ***Tuberculosis- A Gender Assessment in Kenya,*** found out that there is a link between occupation and susceptibility to TB and gender. Key populations for TB such as miners, Matatu crew, truck drivers and boda boda riders are mostly men. Gender is an integral part in the delivery of TB services. In order to have a holistic approach in responding to TB, the government both at the national and county levels needs to embrace the human rights based approach in the delivery of TB services. This will address any gender inequalities, discriminatory practices and any unjust power relations, which may be at the core of TB service delivery.

The current Kenya National Strategic Plan (NSP) on Tuberculosis acknowledges that gender inequalities can impact health risks, health seeking behaviour and responses from health systems, which lead to poorer outcomes. The NSP acknowledges the need to undertake responsive programming, which takes into account the prevailing gender norms or undertakes a gender transformative programming, so as to mitigate harmful gender norms that are barriers to accessing health services. It notes the necessity of conducting active case finding in communities affected by TB, reaching out to women and the poor, who do not have access to services without paying for transportation.

Integrating TB services into Reproductive Maternal and Child Health (RMNCH)-related health services to facilitate access by women and girls is another priority within the NSP. However, there are no interventions targeted towards men (who are disproportionately affected by TB in Kenya) to reduce their barriers to accessing TB services.

The gender related barriers to TB diagnosis, prevention; treatment and care are at the individual level and provider or health system level. Individual level barriers include: health literacy, health seeking behavior, stigma, sociocultural (gender roles and status in the family), financial (the direct and indirect costs of seeking TB services), physical (distance to TB services and access to transport) and treatment adherence ignorance.

Tuberculosis approaches and responses at the international level are anchored in international and regional human rights instruments. These laws recognize that all human beings have equal rights to access quality and timely health services, regardless of their nationality, ethnic origin, sex, race, religion, or any other status and are built around core human rights principles.

17.4.2 Human Rights and Unequal Access to TB Care and Treatment

It is often especially difficult for some key populations to mobilize and demand realization of their rights. For example, migrants face challenges accessing health care in host countries and, in some settings, may face deportation if diagnosed with TB. Miners with TB have the threat of layoffs based on their health status and they face challenges accessing continuous TB treatment and care. Prisoners often experience increased risks of contracting TB due to poor prison conditions and many lack access to good quality services while in detention. Upon release from prison, former prisoners face complications seeking health care and adhering to treatment, as well as stigma and discrimination in their communities. In many countries criminalization of People Who Use Drugs contributes to long delays in diagnosis and lack of case management, leading to treatment disruptions. PLHIV often have access to community support, but the lack of integration of TB and HIV services continues to be a major challenge in the areas of service delivery, human resources and supply of medicines and products.

17.4.3 Criminalization of TB Status: Involuntary Treatment, Isolation, Detention and Incarceration

People affected by TB can be subjected to arbitrary and harmful measures such as involuntary treatment, detention, isolation and incarceration.

According to WHO: "Involuntary isolation, except in narrowly defined circumstances (see below for exceptional circumstances and specific conditions that must be met), is unethical and infringes an individual's rights to liberty of movement, freedom of association, and to be free from arbitrary detention. It is unethical to isolate persons with TB if the person is not contagious or if isolation holds no clear public health benefit to the community."

WHO further specifies exceptional circumstances when involuntary isolation can be considered as the last resort for an individual who is:

i) Known to be contagious, refuses effective treatment, and all reasonable measures to ensure adherence have been attempted and proven unsuccessful

ii) Known to be contagious, has agreed to ambulatory treatment, but lacks the capacity to institute infection control in the home, and refuses care at medical facilities

iii) Highly likely to be contagious (based on laboratory evidence) but refuses to undergo assessment of his/her infectious status, while every effort is made to work with the person with TB to establish a treatment plan that meets his needs.

And **ALL** of the following nine conditions must be met in order to justify any involuntary isolation:

1. Isolation is necessary to prevent the spread of TB
2. Evidence that isolation is likely to be effective in this case
3. Person with TB refuses to remain in isolation despite being adequately informed of the risks, the meaning of being isolated and the reasons for isolation

4. A person with TB's refusal puts others at risk
5. All less restrictive measures have been attempted prior to forcing isolation
6. All other rights and freedoms (such as basic civil liberties) besides that of movement are protected
7. Due process and all relevant appeal mechanisms are in place
8. Person with TB has, at least, basic needs met
9. The isolation time given is the minimum necessary to achieve its goals

Table 17.2: Examples of Human Rights Violations

Rights	Examples of Violations
Right to Life	• Imprisoned or otherwise institutionalized individuals face a disproportionate risk of TB infection, disease and death • People who use drugs, prisoners, other marginalized communities may be denied lifesaving TB treatment and face death
Right to the highest attainable standard of physical and mental health	• Persons with TB are denied access to quality TB treatment and care in prison • Persons with MDR-TB are denied tailored therapies of second-line drugs • Government's failing to utilize donor resources to construct isolation wards • People with TB who belong to additionally marginalized groups are discriminated against in TB care- given subpar treatment or denied care
Right to enjoy the benefits of scientific progress and its applications	• Persons with TB in resource-constrained settings may have limited access to high-quality diagnostic services and first- and second-line medicines for treatment • Poor communities are tested with faulty antiquated tests and consequently over-diagnosed and over-treated. • Restrictive intellectual property regimes limit access to quality, affordable anti-TB medicines
Right to non-discrimination and equality	• Persons with TB are refused medical treatment or given a lower standard of care • Persons with TB are denied and fired from jobs based on their TB status or TB history
Right to privacy	• Information about a person's TB status is disclosed through provider breach of confidentiality, flawed contact investigations, of poor data protections in surveillance systems

Rights	Examples of Violations
Right to be free from torture or cruel, inhuman or degrading treatment or punishment	• Institutional settings are overcrowded or poorly ventilated, making it more likely for individuals to contract TB. • Prisoners are not screened or tested for TB and cannot access medical treatment and care for a TB diagnosis. • Other medicines, such as substitution treatment, are not provided to people with TB who also use drugs in institutional settings • People with TB who are detained are often kept in conditions that may lack access to basic medical services Placing individuals who are arbitrarily arrested in such conditions could constitute cruel, inhuman or degrading treatment
Right to informed consent	• People with TB are involuntarily tested for HIV • Unapproved medication regimens are used to treat people with TB without informing them • People with TB are involuntarily summoned for treatment
Right to information	• People who are illiterate may have less knowledge of TB and its signs and symptoms • Health care workers fail to adequately explain to persons with TB why adherence to TB medicine is important • A comprehensive education program on TB, prevention, signs and symptoms, cure
Right to freedom from arbitrary arrest and detention	• Persons diagnosed with TB, who have been declared to be noncompliant with TB treatment, are arrested • Persons arrested for noncompliance with TB treatment are not provided with treatment while in detention or detained in environments that are non-medical settings (prisons, holding cells, etc.)
Right to a fair trial/ due process	• Individuals with TB are detained without adequate justification that it is the least restrictive alternative, strictly necessary or a measure of last resort
Right to participation	• People with TB and those who had TB have limited opportunity to have a say in designing programmes that aim to support them • Communities of people with TB are not seen as partners in the fight against TB; peer-to-peer approaches are not common in TB care programmes
Right to access of an adequate, effective, and prompt remedy/ representation	• People with TB, especially those from most marginalized communities, may not be able to afford legal aid to seek remedy for their violated rights

17.4.4 Reporting human rights violations in TB

Persons with TB should be empowered to report human rights violations and receive support including linkage to pro bono lawyers for legal aid if it is required.

Human rights violations should be reported to TB champions, health care workers or CHVs who in turn should forward the reports to Sub County TB and Leprosy Coordinators. The TB champions, health care workers and CHVs are also expected to , cases of stigma related violation or discrimination at the facilities, community or HH levels as they go about their work. Sometimes persons with TB may report violations to Non-State Actors working in their communities. The SCTLCs aggregate the data, analyze it and link perosons to the relevant tribunals or escalate to higher levels if need be for resolution. Data will be reported to TIBU through the County TB and Leprosy Coordinator.

17.4.5 Human rights-based TB interventions

These include but are not limited to:

- Training for TB key populations and TB community to increase awareness about TB in relation to human rights.
- Introducing more flexible hours at health facilities that offer TB services, so as to cater for those who work during the morning and day.
- Advocating for collaboration and integration of services- TB, HIV, maternal, neonatal and child health programmes and primary care services to collaborate and integrate to maximise the entry point to TB care for women at all levels.
- Advocating for better data collection regarding women. Advocate for improved recording and reporting of TB data, to be disaggregated by sex and age, including for TB treatment initiation and outcomes.
- Monitoring, documentation and reporting of human rights violations including discrimination, gender-based violence and denial of healthcare services for TB
- Development of community-based monitoring of human rights in TB.
- Routine negotiation, mitigation or formal complaints to challenge actions or inaction of the authorities, state or non-state providers.
- Strategic litigation to bring about changes in policy and legal frameworks.
- Developing strategic partnerships with attorneys, legal clinics, human rights NGOs and academia.
- Training lawyers and healthcare workers on TB, gender and human rights.
- Mass media campaigns
- Conducting active case finding in communities affected by TB, reaching out to women and other economically disadvantaged who do not have means to access services without paying for transportation.
- Utilizing terminologies that are internationally recognized and agreed to by UNAIDS, World Health Organization, STOP TB and other such governing bodies

17.4.6 Patients' charter for Tuberculosis care

The Patients' Charter for Tuberculosis Care (The Charter) outlines the rights and responsibilities of people with tuberculosis. 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 providers a 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 tuberculosis care and enhancing the effectiveness of the healthcare process. It allows for all parties to be held more accountable to each other, fostering mutual interaction and a "positive partnership."

17.4.6.1 Patients have the right to:

i. Care

The right to free and equitable access to tuberculosis 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 multidrug-resistant tuberculosis (MDR-TB) or tuberculosis-human immunodeficiency virus (HIV) coinfections 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 programs.

ii. 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 healthcare in a dignified environment, with moral support from family, friends, and the community.

iii. Information

The right to information about what healthcare services are available for tuberculosis 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 authorized by the patient.

The right to meet, share experiences with peers and other patients and to voluntary counseling at any time from diagnosis through treatment completion.

iv. 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 programs without compromising care.

v. 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.

vi. 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.

vii. Organization

The right to join, or to establish, organizations of people with or affected by tuberculosis 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 tuberculosis policies and programs with local, national, and international health authorities.

viii. Security

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.

17.4.6.2 Patients' Responsibilities

i. Share Information

- The responsibility to provide the healthcare giver 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 tuberculosis or may have been infected by contact.

ii. 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.

iii. 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 tuberculosis.
- The responsibility to show consideration for the rights of other patients and healthcare providers, understanding that this is the dignified basis and respectful foundation of the tuberculosis community.

iv. 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 tuberculosis free.

17.4.7 Guiding principles for implementing TB control activities at the workplace

Stigma and discrimination in TB act as barriers to accessing treatment care and support. People who fear losing their jobs or being kicked out of school because of TB are less likely to seek testing and treatment for the disease. As such, stigma and discrimination are human rights vilations and lead to inequalities in population health.

All employers involved in TB prevention and care should respect the following guiding principles for TB control at work places, especially the health staff in contact with the affected employees.

17.4.7.1 Protect Rights of employees with TB

- **Always respect the rights of employees with TB** - Maintaining the confidentiality of medical conditions and TB/HIV medical records is crucial to giving employees confidence to undergo treatment. Lack of confidentiality can lead to discrimination as well as delayed diagnosis and treatment. Confidentiality means that only the staff directly involved in the individual employee's medical care and know that employee's TB/HIV medical status, have access to his or her records. Medical staff should never divulge the medical status of employees to any other worker or to the management. They should give guidance to line management only on whether employees will need time off and whether there should be any change to their workload and tasks because of their health status. Options should be offered for DOT that respect the rights of the employee with TB. There needs to be a clear statement of policy on the importance of confidentiality, including the consequences of breaking confidentiality where TB/HIV health status is concerned.
- **Offer social welfare benefits to employees with TB and their families** — Social welfare provided to workers and their families can help patients complete their treatment. Welfare benefits may consist of free treatment and services, maintaining salary during treatment (or providing compensation for loss of income) and food support. Importantly, to motivate the employee with TB to continue treatment, social support should be adapted to the delivery and duration of the treatment.
- **Help employees with TB to tailor their workload/tasks to their state of health** — For at least the first 2–4 weeks of TB treatment, an employee with TB should be on leave of absence, with DOT arranged for his or her convenience. The employee may often then resume work, if necessary with an adjusted workload and modified tasks until fitness returns. For example, it may be possible for an employee who is normally engaged in heavy labour to do office work for a few months.

17.4.7.2 Ensure a safe workplace environment

- **Use education campaigns to decrease stigma** — Effective health education campaigns should address negative attitudes towards people with TB. Traditionally TB is viewed as a deadly disease of the poor, and the strong social stigma it provokes makes it more difficult for people with TB to seek diagnosis and treatment. This can be countered by greater knowledge and understanding. For example, education should stress that everyone is vulnerable to TB, that most people with TB cease to be contagious after 2–4 weeks of treatment, and that the disease is usually curable. Education campaigns should not only target TB infected patients only but also the TB/HIV patients who face stigma many a times.
- **Develop and implement clear management policies** — The employer's policies on confidentiality, discrimination, length of time off allowed for medical treatment, and job modification when necessary should be clearly outlined and made easily accessible. They should be clearly explained to employees with TB as soon as such employees are identified and should ensure prompt recognition and referral of TB presumptive employees. Reducing the delay between onset of symptoms and diagnosis and treatment is crucial to decreasing the risk of TB transmission.

- **Implement environmental controls** — Environmental control of TB refers to implementing environment-associated interventions to prevent or reduce airborne transmission from unsuspected cases or from diagnosed cases of TB to non-infected employees. Most TB cases are result of airborne transmission of infection. Environmental factors that enhance TB transmission are:
    i) Small, enclosed spaces
    ii) Areas that lack sufficient ventilation to clean the air through dilution or removal of infectious droplet nuclei
    iii) Ventilation systems recirculating air.

The overall objective of cost-effective interventions in the workplace should therefore be to control the spread of TB by minimizing the concentration of airborne infectious droplet nuclei. Achieving this requires systems that ensure a high flow of fresh air into the workplace environment. It also involves keeping away from other workers with active TB until 2–4 weeks after starting treatment.

17.4.7.3 Use partnership for buy-in

Ensure collaboration with the DNTLD-P. Negotiate and implement TB control activities with all partners. Additionally, it is particularly important to work with workers' organizations to maximize awareness and understanding of the disease and of the programme of control activities.

17.4.7.4 Protecting Human rights in learning institutions and at workplaces

i. Rights violation for a child confirmed to have TB in school

1. Pupils/Students confirmed to have TB need to go home seek for treatment so as not to expose other pupils to Tuberculosis.
2. Once the doctor confirms that the child is no-longer infectious, the pupil or student needs to go back to school as he/she continues with medication.
3. If the school refuses to admit the pupil/student, this amounts to rights violation, let the parent/guardian discuss this violation with the school principal.
4. If the school principal is reluctant to admit the child, the parent/guardian can escalate the violation to the sub-county officer of education.
5. Continue to the county education officer if the violation is not resolved at the sub-county level.
6. Report the issue to court if not resolved at the sub-county and county levels.

ii. Rights violation at workplace

1. Patient/ worker needs to seek treatment so as to avoid putting the co-workers at risk
2. Go back to work once doctor confirms that worker is no-longer infectious
3. If not re-admitted to work, seek to discuss with authority- senior management
4. If not resolved, report to the industrial and Labour court for wrongful termination
5. At the high court, patient can file for discrimination on health status and seek to be compensated

iii. Rights of Health Care Workers in the TB clinic

- Health care workers should have a safe working environment, receive adequate training and support, have adequately equipped facilities and access to quality and regular supplies, including adequate protective measures and equipment, and legal protection.
- Health care workers should be screened for TB at least twice a year.

17.4.8 Leprosy and human rights

Leprosy affects the poorest and most disadvantaged members of society. People with leprosy and their family members suffer stigma and discrimination due to deep-seated misconceptions that have revolved around the disease throughout history. This is despite leprosy being one of the least contagious communicable diseases affecting humans. People with leprosy undergo human rights violations including denial of access to work, education and community life.

17.4.8.1 Principles and Guidelines for elimination of discrimination against persons affected by leprosy and their family members

Adopted in 2010, the Principles and Guidelines for elimination of discrimination against persons affected by leprosy and their family members outline the basic human rights of persons affected by leprosy and their family members and provide the responsibilities of States to promote, respect, protect and ensure the full realization of all human rights for all persons affected by leprosy and their family members

Principle 1: Persons affected by leprosy and their family members should be treated as people with dignity and are entitled, on an equal basis with others, to all the human rights and fundamental freedoms proclaimed in the Universal Declaration of Human Rights, as well as in other relevant international human rights instruments to which their respective States are parties.

Principle 2: Persons affected by leprosy and their family members should not to be discriminated against on grounds of leprosy or having had leprosy.

Principle 3: Persons affected by leprosy and their family members have the same rights as everyone else with respect to marriage, family and parenthood

Principle 4: Persons affected by leprosy and their family members have a right to citizenship and obtaining identity documents.

Principle 5: Persons affected by leprosy and their family members have a right to serve the public, on an equal basis with others, including the right to stand for elections and to hold office at all levels of government

Principle 6: Persons affected by leprosy and their family members have a right to work in an inclusive environment

Principle 7: Persons affected by leprosy and their family members have a right to be admitted to schools or training programmes

Principle 8: Persons affected by leprosy and their family members have a right to develop their human potential to the fullest extent, and to fully realise their dignity and self-worth

Principle 9: Persons affected by leprosy and their family members have a right to be, and should be, actively involved in decision-making processes regarding policies and programmes that directly concern their lives.

ADVOCACY AND COMMUNICATION

18

18.1 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 policies and guidelines 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 which devolved and placed under the management of the county governments under the leadership of the governors and the county health executives. 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 Program must be directed to the county level. The advocacy guideline, 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.

KEY HIGHLIGHTS:

Patient - Key information

- **Effective education is the cornerstone for achieving high treatment success rate.**

Differentiated Communication approaches

- **Target communication with specific channels is essential in TB control**

The program will focus on three main types of advocacy to bolster political commitment, leverage resources, and positively change policies and administrative guidelines:

- **Policy advocacy-** to lobby national and county political leaders to increase funding for TB programs and policy changes for smooth implementation of the activities.
- **Program advocacy-** to reach out to decision-makers and community partners to boost their participation in local actions and program decisions to support TB services.
- **Media advocacy -** to put TB issues on the public agenda, prompt media to cover TB related topics regularly and responsibly to raise awareness of TB problems and solutions.

At the national level, the program head together with the Stop TB partnership will work together on strategies to lobby parliamentary caucuses on TB, treasury, Ministry of health and 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 various partners will work on strategies to ensure branding of the National TB 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 / County Executive Committee (CEC) for health and County Health Management Team (CHMT) will work on strategies to lobby the County government to ensure that TB, Leprosy and Lung Disease activities are included in the county integrated development plan and resources allocated in annual work plans and budgets. The activities/events to be lobbied for consideration should include the following but not limited to, World TB day, World Asthma, World and Leprosy day.

At the community level the community health extension workers together with Community health volunteers and Civil society organizations will work on the strategies to advocate for communities to demand for TB, Leprosy and Lung Disease treatment and care at the community level.

At the National and County level, the private sector will be engaged to support the implementation of Advocacy Communication and Community Engagement strategies. The advocates should endeavor to reduce the cost of treating and caring for TB, Leprosy and Lung disease through the waiver system, NHIF or other existing insurance companies.

18.1.1 Planning for advocacy sessions

Planning for an advocacy campaign is a dynamic process. It involves identifying the issue, developing solutions, building support, and bringing issues, solutions and political will together to ensure that the desired change takes place. It includes the following steps;

1. Researching on the issues and setting objectives
2. Gathering evidence

3. Identifying target audience
4. Identifying allies
5. Developing message
6. Planning how to deliver the message
7. Raising resources
8. Monitoring and Evaluating the impact of advocacy activities

18.1.2 Strategies for Advocacy

- **Coalition building -** Coalition building refers to alliance or partnership of the TB program and other stakeholders in order to achieve a common purpose or to engage in joint activity. It brings more expertise and resources to bear on complex issues.
- **Dialogues -** This an informal and amicable strategy that entails talking to a person or entity of influence with a view to influencing or persuading them
- **Petitions -** This is a strategy through which people are allowed to raise their concerns or complaints to those in authority. In often cases, it is usually in writing with the petitioners appending their signatures.
- **Processions -** These are lawful and peaceful demonstrations with a view to sensitising on an issue that affects the public and one that they are not happy with.
- **Public Interest Litigation -** This is a strategic case which is usually filed to address issues of public concern or to advance human rights and equality
- **Picketing -** This is a peaceful protest where members of the public congregate. This is done to draw attention to a cause.

18.2 Communication

Health Communication is aimed at promoting health care seeking behaviour, prevention in the community and promoting innovative patient-centered communication methods in line with the 2019-2023 NSP and 2020 ACCE for TB, Leprosy and Lung Health.

Communication plays a vital role in changing knowledge, creating awareness/positive attitudes and improving the practice of positive health behavior. It should aim to create awareness at all levels in the care continuum; policymakers, health care workers, community and patients, in order to change attitudes and behaviors leading to a Kenya free of TB, Leprosy and reduced burden of lung diseases.

18.2.1 Justification for communication strategies

In the last few years, whilst a number of resources have been expended in the development of various IEC materials, there still exists a huge gap in terms of TB awareness. According to the prevalence survey (2016), it was found that there was limited awareness of the cardinal signs and symptoms of TB, and many people either do not recognize these symptoms as symptoms of tuberculosis, or do not take the requisite actions whenever they experience them. This results in patient delays in seeking care and enhances continued active transmission further compounding the TB menace.

Misconceptions, myths and stigma amongst populations also contribute highly to poor health seeking behavior which is a huge impediment to TB care and treatment due to its high correlation to HIV. This results in negative impact in drug adherence for those already in care and further discourages screening and testing. According to the Legal Environment Assessment for Tuberculosis in Kenya (KELIN, 2018), stigma has led to limited uptake of TB preventive therapy (TPT) and other care services. Varying knowledge and understanding of TPT among both the community and HCWs has also hampered uptake. In addition, the influx of enrolment in learning institutions without commensurate infrastructure has led to limited infection prevention control measures.

18.2.2 TB related communications falls into three categories:

- **Mass media -** this includes radio and or television advertising campaigns, digital media and social media, websites, special events and behavior change communication campaigns that reach a general and targeted audience.
- **Small media -** also referred to as information, education, and communication (IEC) approaches. It includes targeted channels, like brochures, posters, mobile phones, photography, video, interactive theater, and testimonials to reach specific groups.
- **Interpersonal communication** - this includes counseling, one-on-one education sessions, skills training, and presentations that target health workers and direct supporters of TB patients and families.

18.2.3 The objectives of health communications should be aimed at:

1. Increasing knowledge on TB disease and control services
2. Increasing knowledge on Leprosy and Lung diseases
3. Changing attitudes and behaviours of clients/patients (current and potential), health providers, and the community (general population).

To achieve this goal, multimedia and targeted (differentiated) communication approaches will be used. It will be combined with mass media, social media and interpersonal media so that all key populations are reached.

The table below describes differentiated Communication approaches on prevention, treatment and care.

Table 18.1: Differentiated Communication approaches

Audience (Primary target)	Message	Objective	Channels
Caregivers (Children under 5years)	**Address Facts on TB (Leprosy/ Lung Diseases) which include:** **What TB is:** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen and side effects of the medication	To promote uptake of screening and testing Reduce stigma surrounding TB Reduce the spread of TB To increase treatment adherence To ensure treatment success-rate	Social Media Digital Media Mass Media (TV and Radio) Outreach programs (roadshows, concerts, mobile screening) Out of Home messages (wall and matatu branding) One on one discussion
Young men and women (age 24-35)	**Address Facts on TB which include:** **What TB is:** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?**	To promote uptake of screening and testing Reduce stigma surrounding TB Reduce the spread of TB To increase treatment adherence To ensure treatment success-rate	Social Media Digital Media Mass Media (TV and Radio) Outreach programs (roadshows, concerts, mobile screening) Out of Home messages (wall and matatu branding)
Women and men aged 65+	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen	To promote uptake of screening and testing Reduce stigma surrounding TB Reduce the spread of TB	Vernacular radio and TV Religious institutions *Chamas* Community outreach (religious led mobile screening, market screening)

Audience (Primary target)	Message	Objective	Channels
School / University students	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen **Peer to peer screening**	To promote screening and testing Reduce stigma surrounding TB Reduce the spread of TB	Social media Digital media Out of home messages (festivals, concerts) Peer to peer outreach (training students to reach out to peers) Radio
Patients/ clients	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen and side effects of the medication **Treatment Adherence**	Increase awareness Promote adherence to medication To promote uptake of screening and testing Reduce stigma surrounding TB Reduce the spread of TB	IEC materials (Posters / brochures) Social media Digital media Health care channels Health care workers Patient support groups
Key populations (refugees, prisoners and PLHIV)	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?**	Increase awareness To promote screening and testing Reduce stigma surrounding TB Reduce the spread of TB	Outreach programs (interpersonal communication)

Audience (Primary target)	Message	Objective	Channels
Community/ Family Members	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen and side effects of the medication	Increase awareness To promote screening and testing Reduce stigma surrounding TB Reduce the spread of TB	IEC materials (Posters/brochures) Health care workers Digital media Social media Mass media Outreach programs (roadshows, concerts, mobile screening) Out of Home messages (wall and matatu branding)
Health care workers and public health Public Health Officers	Anyone can get TB Screen all patients Importance of patient follow up and management Continuous medical education is key to TB management and treatment Importance of contact tracing Importance of patient counseling	Uptake of screening/TPT among HCWs Increase case detection Ensure treatment success rate Reducing the spread of TB	SOPs Training forums Health care channels IEC (Posters / brochures) Digital media (TIBU, ECHO) Social media
Informal Health Service Providers (ISPs)	**What is TB?** Prevention, symptoms and modes of transmission. **How is TB treated?** Treatment regime Anyone who is symptomatic should be referred to health facility	Patients' referrals. Reducing the spread of TB. Increase case detection. Increase formal health-seeking behaviours. Promote TB treatment and management.	Screening tools Posters Trainings

Audience (Primary target)	Message	Objective	Channels
Audience (Secondary Target)			
Learning institutions' administration and management	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Providing proper infrastructure to stop the spread of TB** **Myths and facts about TB** **How is TB treated?** **Importance Screening of Students**	Increase knowledge to be able to screen and identify presumptive cases Educate and empower school fraternity on TB management To promote uptake of screening and testing services Reduce stigma surrounding TB Reduce the spread of TB	Circulars from Ministry of Health and line ministries Brochures Trainings and meetings Out of home messages (talking walls)
Private sector	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Providing proper infrastructure to stop the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen **Screen all employees** **Resources and collaboration to fight TB and Lung diseases**	Increase knowledge to be able to screen and identify presumptive cases Educate and empower leadership to enforce TB management To promote uptake of screening and testing services Reduce stigma surrounding TB Reduce the spread of TB	Stakeholder forums Outreach programs (workplace screening) Brochures / posters Pay slips Email signatures Internal communication structures
Private Insurance companies	Proper diagnosis of TB saves money because of fewer doctor visits and prescriptions	To include TB screening in health care packages	Meetings Emails

Audience (Primary target)	Message	Objective	Channels
Funding partners	The TB and Lung health situation in the country, highlighting the funding gaps and need for more resources	Resource mobilization	Reports Emails Case studies / newsletters Meetings Documentaries
Champions and advocates	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** Treatment regimen	Give champions and advocate correct information about TB to spread the message.	Trainings Meetings Digital media Social media Brochures
Line Ministries, Governors, President and local and national leaders	The importance of resource mobilization There is a TB and lung health problem that needs to be addressed We need to work together to end Tb in Kenya	Allocate more resources towards improving TB and lung health response	Circulars Posters Digital Media Meetings Emails Ministry publications
Policymakers: Parliamentar-ians, Senate, MPs and MCAs	The importance of resource mobilization There are TB and lung health problems that needs to be addressed We need to work together to end TB in Kenya	Allocate more resources towards improving TB and lung health response	Meetings Reports
DNTLD-P Program Managers	Importance of the communication function in awareness creation Importance of resource mobilisation	Allocate more resources both personnel and financial towards demand creation and awareness	Emails Memos Meetings WhatsApp

Audience (Primary target)	Message	Objective	Channels
DNTLD-P program staff	Importance of the communication function in awareness creation Importance of sharing successes and stories	The need for different departments to work together to create demand creation and awareness	Posters Meetings WhatsApp Emails Social media Digital media
Opinion Leaders: religious leaders, community elders	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** The importance of mobilization There are TB and lung health problems that needs to be addressed We need to work together to end TB in Kenya	Mobilization to spread awareness about TB and lung health	Inter-personal communication Brochures / Posters Banners Out of home messages (wall branding) Training
CSOs and supporting partners	The TB response in Kenya is led by NTLD, with partners working collaboratively	Gaining technical support from partners	Technical working groups Meetings Emails
Media	**What is TB?** Prevention, symptoms and modes of transmission. **TB is curable and treatable:** TB screening and treatment is free in all government facilities. **Anyone can get TB** **Preventing the spread of TB** **Myths and facts about TB** **How is TB treated?** **Why is TB a priority now? How does TB impact Kenya**	Spread awareness about TB To promote uptake of screening and testing Reduce stigma surrounding TB Reduce the spread of TB	Trainings (media engagement) Reports Digital media Social media

Communication on Prevention (as per the table above)

The areas to focus on are:

- Facts on TB (frequently asked questions on TB)
- Facts on Leprosy (frequently asked questions on leprosy)
- Facts on Lung Health (frequently asked questions on lung health)

18.2.4 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 with 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.

Communication is key in improving patient adherence. Health care workers should consider a variety of factors and implement strategies targeting underlying issues. The strategies should include customizing and simplifying all learning and intervention regimens, identifying and addressing barriers to adherence, ensuring patient support structures are in place for ease of communication, and improving self-efficacy and health literacy among all key stakeholders.

HCW knowledge gap - There is a need to sensitize HCW to understand the implications of TB, DR/MDR/XDR-TB treatment challenges and public health ramifications.

18.2.5 Health Informational support

Any useful information that helps a person to solve problems and address sources of stress e.g. training, IEC materials for patients should be shared through the patient's most preferred medium. The information should be on:

- What healthcare services are available for tuberculosis and what responsibilities, engagements, and direct or indirect costs are involved
- How 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 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 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 authorized by the patient

- The need to meet and share experiences with peers and other patients and to voluntary counseling at any time from diagnosis through treatment completion

Patients have a responsibility to provide the healthcare givers with as much information as possible about present health, past illnesses, any allergies, and any other relevant details. The information should also include contacts with immediate family, friends, and others who may be vulnerable to TB or may have been infected by contact.

The community has a right to access and understand information about TB, DR/MDR/XDR-TB, its causes, its implications on their health, and the internationally recommended standards and policies for prevention, diagnosis and treatment. People should participate actively in decisions related to what is being done to their bodies and to the samples obtained from their bodies, and why it is being done. This may help to instill trust in the health system.

Some of the key interventions in reducing the non-adherence to treatment include:

1. Innovative health communication
2. Use of digital health platforms
3. Social support mechanisms
4. Health Education
5. Treatment plan

18.2.6 Patient Education and Informed Consent

All TB patients and their primary caretaker(s) should receive education about TB and its treatment and the need for adherence. Adjustments in the attitudes and language used by healthcare providers while delivering key information about the disease should be applied.

- Information and education interventions should commence as soon as diagnosis is made and continue throughout the course of treatment.
- Education can be provided by: physicians, nurses, community health workers and other health care providers/stakeholders, Pharmacists, CHWs, Counsellors, Peer educators, Social workers, DOT supporters and others.
- Materials should be appropriate to the literacy levels of the patient and should be gender, age and culturally sensitive.
- All health care providers should adopt methods of 'communicating with' (and not 'talking at') patients and their caretakers
- For patients with literacy limitations, efforts should be undertaken to use e-health tools based on audio or visual support.
- Patient education should be continuous in the course of treatment

18.2.7 Communication on Post TB treatment

Meaningfully engage the willing and cured TB survivors in efforts towards awareness creation and demand creation for TB health services, Leprosy and Lung Disease. This can be through telling their stories of determination and using them as champions in messaging both online and offline.

18.2.8 TB control challenges that can be addressed through ACCE include

- Delayed detection and treatment,
- Lack of access to TB treatment,
- Difficulty in completing treatment,
- Stigma and discrimination that can prevent people from seeking care and diagnosis,
- Lack of knowledge and information about TB, leading to stigma, discrimination and delayed diagnosis and/or treatment,
- Misunderstandings and myths surrounding TB, including the belief that it is "untreatable",
- Failure to understand the link between TB and HIV, with the view that having TB means one has HIV,
- Weak political support for TB programmes.

18.2.9 Each patient must understand what the treatment entails:

- Different medicines,
- Duration,
- Possible side-effects,
- Importance of completing treatment and taking every medicine as prescribed
- Possibility of HIV co-infection and treatment.

The educator must verify that the patient has fully understood the message by asking the patient and the DOT supporter to explain the information in his/their own words.

18.2.10 Principles of patient education

- The first IEC session should focus on acceptance of the diagnosis;
- Assume that each patient with TB will be worried about having HIV (unless they already know their status), and that not addressing this represents a missed opportunity for HIV prevention and patient management.
- Education is a dialogue, not a lecture.
- Involve patient companions (family, relatives and friends) in the education sessions to maximise retention and reinforcement.
- Always encourage the patient and his/her companions or treatment supporter to ask questions.
- The educator should try to put himself in the position of the patient.
- Allow sufficient time for each session.
- Use several approaches repeating the same messages: group discussion, individual dialogue, leaflets, flip-charts etc.
- Provide the patient and his companions with information leaflets in the language they can read and understand. Verify that the patient has understood the message(s) by asking him/her to repeat the message(s) in his/her own words
- Avoid providing too much information at the same time.
- Repeat education sessions if possible.

18.2.11 Key information

Effective education is the cornerstone for achieving high treatment success rate and preventing the spread of TB and reduce treatment defaulting.

Table 18.2: Summary of Key information

What patients and his/her DOT supporter needs to know	• TB is curable, if treatment is taken as prescribed • TB treatment is available free of charge at any government or mission health facility. • TB is an infectious disease that is transmitted from one person to another by coughing, and appropriate cough hygiene reduces transmission. • The patient may already have infected other people who may also develop TB. The patient should therefore encourage other people with whom s/he is in close contact to have themselves checked for TB disease now and when become ill or display symptoms. • It is important to identify a DOT supporter and determine where and when medication will be administered. • All close contacts under 5 years of age and HIV infected contacts are at high risk of suffering TB disease if infected and can benefit from TPT. • The duration of initial and continuation phases of TB treatment must be explained (give the actual duration to the patient and verify that they understand).

	• Explain which pills s/he will take during the full treatment course; show and explain number, colour and frequency. • Once treatment with these medicines has begun, symptoms of TB disease will disappear quickly; but the medicines still need to be continued daily until the end of the prescribed treatment period. • Failure to adhere to this treatment may cause TB disease to start again, with great risks for the health of the patient, because the second time around the treatment is likely not to work as well. In particular, there is a risk of developing drug resistance and transmitting the disease further to others. • Because of the risk of transmitting TB to the community, it is the patient's responsibility to complete the TB treatment the first time. Interrupting treatment puts the community at risk. • Sputum-smear examinations are required at certain intervals to monitor the progress towards cure. • TB and HIV are different diseases, but HIV is common in TB patients. • TB can be cured, even when you have HIV. • It is important for the nurse or doctor and the patient to know the patient's HIV status so that the patient can have access to better treatment, including ART
	During treatment • Re-emphasise the need for follow-up visits and investigations • Patient should inform the staff at the clinic when s/he intends to travel. An adequate supply of medicines can then be given to cater for the period of travelling • Patient should inform the staff at the clinic when s/he intends to move to another area. The clinic staff will then write the transfer letter and give advice as to where treatment can be continued
	At the end of treatment • TB may occur again, especially if one is HIV positive; • The patient should report immediately to the TB clinic, when s/he notices similar symptoms, to be examined for recurrence of the disease. • It is important to maintain a healthy lifestyle, even after TB treatment.

What the community should know	• Kenya is one of the worst TB epidemics in the world. • TB is caused by type of bacteria (germs) that are passed on from one person to another through the air, and is not caused by witchcraft, dust, sharing utensils or inheritance. • Everybody who has a cough of any duration, or has coughed up blood should go to a clinic or hospital to have his/her sputum examined for TB. • TB treatment is free of charge in government and mission health facilities. • TB can be cured completely if you come early when you are ill and take the treatment to the end. • TB patients who are not on treatment are spreading TB disease within their families and communities. • TB patients on treatment are not infectious and do not need to be isolated or shunned; but rather need support and encouragement to complete their treatment. • There is no danger in being close to a TB patient who is on TB treatment: touching, sleeping, and sharing food or eating utensils is safe.

	• TB and HIV are different diseases, but HIV is common in TB patients. Most patients with TB in Kenya do not have HIV. • TB can be cured, even when a person has HIV. • All TB patients should have an HIV test, so that those who are HIV positive should be treated for HIV. • Community members should identify friends and colleagues with chronic cough, weight loss, and prolonged fever and advise them to be screened and tested for TB as soon as possible. • People should cover their mouths when they cough (cough hygiene), preferably with the inner part of the elbow, a handkerchief or tissue paper. • Houses, barracks and correctional facilities and public transport should be kept clean and well ventilated, with windows kept open as much as possible. • Houses should have wide windows for ventilation and sunlight. • Avoid overcrowding in correctional facilities, hostels, barracks and private homes, if possible
What leadership can do in the fight against TB	• Include TB in their health agenda and ensure that the health agenda is represented in every sector. • Stress the importance of fighting TB which is a widespread disease but is very curable. • Allocate sufficient human and financial resources to fight TB. • Mention the need to fight TB in public addresses. • Stress that TB and HIV often go together - but not always, and that every HIV infected patient should be regularly screened for TB, while every TB patient should be tested for HIV in order to access life- saving HIV treatment if HIV positive • Be sincerely committed to fighting poverty and HIV, as both are fueling the TB epidemic. • Ensure social protection for patients, families and communities affected by TB; they must be prevented from suffering economic losses because of TB.

19

ENGAGING COMMUNITIES, PATIENTS, AND NON-STATE ACTORS (NSA) IN TB, LEPROSY, AND LUNG HEALTH CARE SERVICES.

Target audience and purpose

This chapter on community engagement will be useful in implementing Tuberculosis and Leprosy interventions. It provides a simplified, step-by-step operational guidance to the community engagement and outlines the critical community-related processes that would make implementing interventions successful and impactful. Further, it will support the ministry of health, county government health departments, non-state actors, funding agencies and research stakeholders, and the community at large as they participate in implementation. Innovative community engagement strategies should also be adopted and replicated in Leprosy & Lung health interventions.

Key terms and definitions

Key term	Definition
Community Members	These are the various members of the community, including but not limited to: Patients, household members (adults and children), community health workers, and community leaders.
Community	The community refers to the level of care in which patients seek services from the Community Health Volunteers/workers and Community Health Extension Workers who provide preventive, promotional, and basic curative care services while linking and referring community members for the appropriate health services.
Community Unit	A "community unit" as defined in this context comprises approximately 1,000 households or 5,000 people who live in the same geographical area, sharing resources and challenges. Each unit is assigned two community health extension workers (CHEWs) and ten community health volunteers (CHVs) who offer promotive, preventive, and basic curative services. Each community unit is linked to a primary healthcare facility.

Community Strategy	It is the mechanism through which households and communities strengthen their role in health and health-related development by increasing their knowledge, skills, and participation.
The Household	The household-level consists of individuals associated with and usually headed by the household head or caregiver. Also can be defined as members of households and families who are both the primary targets and implementers of level one services. They are responsible for the day-to-day upkeep of the household affairs as well as participation in community-organized health activities. They are in contact with the CHVs and formal health system where they seek and utilize health services. The household forms the first level of care that is universally available.
Community Owned Resource Persons (CORPS)	CORPS are persons that exhibit good leadership, have been in the community for a relatively long time, and have a close relationship with the community. They understand and believe in the health initiatives' goals, their respective community (architecture) environment, systems, and structures and hence will largely have an impact and influence on community behavior.
Community-Based TB, Leprosy and Lung Health Services	This refers to the provision of TB services outside the premises of formal health facilities (e.g., hospitals, health centers, dispensaries, and clinics) in community-based structures (e.g., schools, places of worship, congregate settings) and homesteads.
Non-State Actors (NSAs)	NSA is the public benefit organizations, including Non-Governmental Organizations (NGOs), Civil Society Organizations (CSOs), and community-based Organizations (CBOs). Faith-based Organizations (FBOs) and other organizations supporting the community outside the government.
Stakeholders in the Community	Stakeholders are those involved in program operations, management, program staff, partners, funding agencies, Patients or clients, advocacy groups, community members, and elected officials.
Multi-sectoral Approach (MSA)	Deliberate collaboration among various stakeholder groups (e.g., government, civil society, and private sector) and sectors (e.g., health, environment, and economy) to jointly achieve a policy outcome.
Multi-disciplinary Approach (MDA)	Involves drawing appropriately from multiple disciplines to redefine problems outside of normal boundaries and reach solutions based on a new understanding of complex situations.
Community Health Committee(CHC)	A community health committee is a committee that comprises a group of selected members who reside in the same community. This committee provides leadership and oversight in the implementation of health and other related community services within the community unit.
Community Health Volunteer (CHV)	The CHV is a member of the local community he/she is selected to serve in. A CHV is selected by the community and undergoes training to prepare him/her to serve households that are organized as part of a community health unit. The work of the CHV is supervised by the CHA/CHEW.

Community Health Assistant/Extension Worker (CHA/ CHEW)	The Community Health Assistant / Extension Worker (CHA / CHEW) is a formal employee of the County Government, forming the link between the community and the local health facility.
Community Strategy	This is a community-based approach, through which households and communities take an active role in health and health-related development issues through increased knowledge, skills, and participation in health matters.
ENGAGE-TB Approach	This is an approach that seeks to shift the perspective of TB from only a medical illness to a more comprehensive socio-economic and community problem. This approach facilitates the engagement of various stakeholders in community TB activities.

Background

Communities are at the foundation of affordable, equitable, and effective health care. The community health approach is an effective means for improving health and contributing to general socio-economic development. Globally, this approach has been recognized as an effective way of making improvements in health care delivery as well as addressing the heavy burden of disease and therefore contributing to health and socio-economic development. Engaging communities on health matters is central to the success of any public health intervention. Thus, community engagement in TB, Leprosy, and lung health involves those affected in understanding the risks/challenges they face as well as involving them in acceptable response actions.

The WHO global post-2015 plan, endorsed at the World Health Organization (WHO), World Health Assembly (WHA) in May 2014, set the target for ending TB by 2035. This plan emphasizes four driving principles to end TB: *strong coalition with Non-state Actors and Communities, Protection and Promotion of human rights, ethics, and equity*. Sustainable development goal 3.3 requires that by 2030, countries should have ended the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases (like Leprosy) and combated hepatitis, water-borne diseases, and other communicable diseases.

In Kenya, Tuberculosis still remains a public health challenge despite the disease being treatable, curable, and preventable. Despite the cost of diagnosis and medicine to treat TB being free for patients in Kenya, men, women, and children are still becoming ill and dying from TB every day. With this in mind, innovative community engagement strategies must be integrated as part of TB interventions to avoid just waiting for patients to present themselves at the health facilities for essential services. On the other hand, Leprosy (which is at the post-elimination phase, according to WHO) continues to affect a significant number of patients. A high percentage of patients are presenting with grade 1&2 disability attributed to delayed diagnosis. Deformities and disabilities often contribute to stigmatization 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 (HCWs) need to

understand the importance of engaging communities & non-state actors (NSAs) in the implementation of respective interventions/activities. Increased and enhanced collaboration between HCWs, communities & NSAs, will lead not only to improved health outcomes in TB and Leprosy (through the provision of an effective continuum of a care package to patients as they exist in the facilities) but also an improved quality of life.

Rationale and Goal for Engaging the Community and Non-State Actors

Though diagnosed in clinics and hospitals, TB and Leprosy thrive in the community. The TB prevalence survey of 2016 showed that there are still missing persons (40%) with TB. Action in the community is therefore essential in the country's efforts against TB and Leprosy. It is therefore important to take a multi-sectoral approach and link community action on TB and Leprosy with the work of the national and county level so that the efforts of the health systems are extended, create demand for quality services, and reach as many people as possible.

There are three critical areas of TB and leprosy programming that are a natural fit for NSAs (NGOs, CSOs, FBOs, etc.) community-level work. As NSAs are often already positioned to serve as a bridge between the health system and the community, they are natural candidates to fill these roles. Health expertise is not a requirement—just a willingness to learn the basics of TB/Leprosy and to link to available TB/leprosy services.

NSAs can assist in:

- **Case finding or case detection**- As people go about their daily lives, at home, work, and school, and participate in cultural, political, economic, and religious activities, there are many opportunities to find out who might have symptoms of TB or Leprosy. Individuals and some groups in the community are in a good position to help identify people with symptoms of TB/leprosy and link them to health care services. Case-finding practices also help find people who have been exposed to TB so that they can receive TB Preventive Therapy (TPT) for latent TB infection.
- **Treatment support**- TB and leprosy treatment entails taking pills regularly over a stipulated period. This can present challenges, including experiencing side effects, forgetting, losing, or running out of medicine, and having social and emotional complications. Treatment supporters help overcome these obstacles. The medicine-taking routine is often easiest when integrated into the patient's everyday life. Historically in Kenya, TB/leprosy patients are expected to report to a health facility every day, week, or every two weeks, depending on the type of TB/leprosy being treated as well as their phase of treatment. Too often, the patient doesn't have the time, energy, and/ or resources to make that daily or weekly or two weekly journey leading to poor adherence. This poor adherence may lead to the patient not getting better, development of drug-resistant TB/ Leprosy in the face of continuing spread in the community.

- **Advocacy, communication, and social mobilization (ACSM)** -ACSM activities help build public knowledge and foster positive attitudes and practices that contribute to efforts to stop TB and Leprosy. Such efforts are most powerfully organized "from the inside" by people who really know and belong to the community. What wrong beliefs do people have about TB and Leprosy? What keeps sick people from seeking help? What pressures, beliefs, and stigmas might be getting in the way? (Stigma is the unfair disapproval or prejudice against a person, in this case, because the person has or may have TB or Leprosy.) What is the best plan of action to create positive change in this community at this time?

In order to synchronize effective TB and leprosy patient care and support interventions, there is a need for enhanced collaboration and coordination between the HCWs, communities, and NSAs. Involving the community and collaborating with its members are cornerstones of efforts to improve public health in relation to TB, Leprosy, and lung health.

Community Engagement

This is the process of working collaboratively with and through groups of people affiliated by geographic proximity, special interest, or similar situations to address issues affecting their wellbeing. Community engagement is a powerful vehicle for bringing about environmental and behavioral changes that will improve the health of the community and its members. It often involves partnerships and coalitions that help mobilize resources and influence systems, changes relationships among partners, and serve as catalysts for changing policies, programs, and practices.

Why Community Engagement for TB, Leprosy, and Lung health?

- **Everyone has a right to know about risks to their health and well-being**
- **Culturally appropriate information can help make informed decisions to reduce the health risks**
- **Action taken by individuals, families and communities affected are key to controlling the public health threat/problem**

Graphic: http://www.dse.vic.gov.au/effective-engagement/introduction-to-engagement/ what-is-community-engagement

Community engagement can also be seen as a continuum of community involvement. The table below illustrates one way of thinking about such a continuum. Over time, a specific collaboration is likely to move along this continuum toward greater community involvement, and any given collaboration is likely to evolve in other ways as well. Most notably, while community engagement may be achieved during a time-limited project, it frequently involves — and often evolves into— long-term partnerships that move from the traditional focus on a single health issue to address a range of social, economic, political, and environmental factors that affect health.

For successful community engagement, there must be an effort to increase the level of community involvement, trust, and communication as shown below

Increasing Level of Community Involvement, Impact, Trust, and Communication Flow

INFORM	CONSULT	INVOLVE	COLLABORATE	SHARED LEADERSHIP
Some community Involvement	More community involvement	Better community involvement	Community involvement	Strong relationship
Provides the community with information	Gets information or feedback from the community	Involves more participation with the community on issues	Forms partnerships with the community on each aspect of the project – from development to solution	Strong partnership structure is formed
Optimally established communication and outreach channels	Develops connections	Visibility of partnership established with increased cooperation	Partnership building, trust-building	Broader health outcomes are affecting broader communities. Strong bidirectional trust built

Approaches Linked to Community Engagement

- Social mobilization
- Behavior change communication
- Health education and promotion

Social Mobilization

This is the process of bringing together all societal and personal influences to raise awareness of and demand for health care, assist in the delivery of resources and services, and cultivate sustainable individual and community involvement.

This process engages and motivates a wide range of partners and allies at national, county, and local levels to raise awareness of and demand for a particular health objective through dialogue.

Members of institutions, community networks, civic and religious groups, and others work in a coordinated way to reach specific groups of people for dialogue with planned messages. Social mobilization seeks to facilitate change through a range of interrelated and complementary players.

Social and behavior change communication (SBCC)

This is an interactive process with communities (as integrated with an overall program) to develop tailored messages and approaches using a variety of communication channels to develop positive behaviors; promote and sustain individual, community, and societal behavior change; and maintain appropriate behaviors. It strategically uses communication approaches to promote changes in knowledge, attitudes, norms, beliefs, and behaviors. This process helps in analyzing the health problem in order to define barriers and motivators to change and design a comprehensive set of tailored interventions that promote the desired behaviors.

Health Promotion and education

This is a set of principles that involve- equity, empowerment, practices encompassing communication, capacity building, and politically oriented activities; aimed at enabling community members to gain more control over the influence of their lives and to improve their health.

- **Health promotion** aims at engaging and empowering individuals and communities to choose healthy behaviors and make changes that reduce the risk of developing TB, Leprosy and other lung related morbidities. It enables people to increase control over their own health. It covers a wide range of social and environmental interventions designed to benefit and protect individual people's health and quality of life by addressing and preventing the root causes of ill health, not just focusing on treatment and cure.
- **Health education** aims to provide information to influence the peoples' future decision-making on their health. It provides learning experiences on TB, Leprosy and lung health while presenting information to target populations on particular aspects of TB, Leprosy and lung health, including the health benefits/threats they face, and provides tools to build capacity and support behavior change in an appropriate setting. Health education looks at the health of a community as a whole, seeks to identify TB, Leprosy and lung health issues and their trends within a population, and works with stakeholders to find solutions to these concerns.

Principles of community engagement

i. Planning phase

- Clarify purpose/goal.
- Understand the community's culture, perception, economic condition, social networks, political and power structures, norms, values, demographic trends, history, and past experience.
- Establish relationships, build trust, work with formal and informal leaders, and seek their commitment for mobilizing the community.
- Map and leverage existing community engagement mechanisms, e.g., for TB, Leprosy, Polio, immunization campaigns, HIV work, Red Cross volunteers, etc.

ii. Implementation Phase

- Collaborate with the community to create change and improve health.
- Recognize and respect diversity, and ensure that the most vulnerable are reached and engaged.
- Identify, mobilize assets and strengths in developing the community's capacity and resources to make decisions and take action
- Be prepared to release control actions and interventions to the community. Be flexible to meet the changing needs.

Challenges Related to Community Engagement

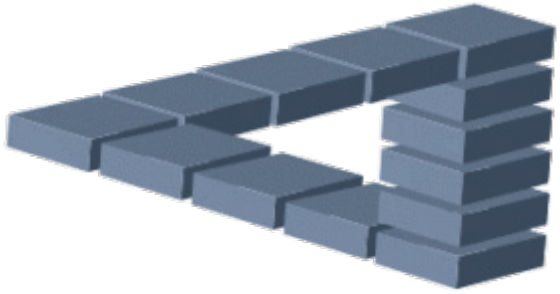
- Maintaining community involvement over time.
- Overcoming differences between the healthcare team, community, individual members of the community, and different influencers.
- Working with unique, especially vulnerable, or hard to reach communities.
- Communities, individual members of the community, and healthcare teams may not perceive risk in the same ways.
- Communities have complex social dynamics and changing power relationships, which influence how we engage them.

Know the community

- Community structure
  - Formal and informal
  - Opinion leaders and influencers
- Community dynamics
- Power relationships
- Sources of information
- Beliefs and practices
- Available resources
- Other important aspects of the community

The Perception Trap in Relation to Community Engagement

The perception trap is real and can make or break a public health intervention. Distorted and fixed perceptions are dangerous. Our communities are becoming more complex, integrated, and agile, and that static points of view limit our ability to collect information, synthesize it, and have meaningful engagement. Holding onto a narrow view means the community, and we make mistakes because our actions are based on incomplete knowledge. Convinced in our accuracy, we refuse to adjust our views or consider other options. Instead of listening to different points of view, we prefer to have others just agree with us. When the community or we realize that those we are engaging have their mind made up, we stop sharing information since it becomes a waste of their or our time. How many ways do you see this image?



Optical illusions have several ways they can be perceived. How open are you? Apart from the community-related perception traps, do you have some yourself? Just as we get our eyes examined to see clearly, we must also test our perceptions. For as Thoreau noted- "It's not what you look at that matters, it's what you see." We must continually test our perception before we accept what we see at first glance is all that there is to see as we engage communities on matters of health.

As one engages the community, it is worth putting into consideration some of the perception traps that may exist in the community and upon self in order for these to be addressed; below is an example of a perception trap related to TB-

TRAP 1 - Fear: TB= HIV + Death

- Everyone who has TB has HIV
- Everyone who has TB will die
- TB is a curse or is due to being bewitched

TRAP 2 - Dismissal

- Don't want to know
- Don't want to believe
- Don't want to accept

TRAP 3 - Disbelief due to distrust

- TB is not curable
- TB cannot be prevented.

The table below provides a summary of important key points to remember during community engagement

1. Communities must be at the heart of any public health intervention especially if we are to end TB and Leprosy.
2. It is critical to know and understand communities in-order to effectively work with them in all phases of health interventions.
3. Multiple strategies and tactics should be used to engage communities
4. Community engagement is grounded in the principles of community organization: fairness, justice, empowerment, participation, and self-determination.
5. To achieve successful collaboration with a community, all parties involved need to strive to understand the point of view of "insiders," whether they are members of a neighborhood, religious institution, health practice, community organization, or public health agency Key to developing such understanding is recognizing one's own culture and how it shapes one's beliefs and understanding of health and illness.
6. Meaningful community participation extends beyond physical involvement to include generation of ideas, contributions to decision making, and sharing of responsibility.
7. Developing a constituency, or developing relationships with community members who have a stake in and support public health and health care, involves four "practice elements":
    - Know the community, its constituents, and its capabilities.
    - Establish positions and strategies that guide interactions with constituents.
    - Build and sustain formal and informal networks to maintain relationships, communicate messages, and leverage resources
    - Mobilize communities and constituencies for decision making and social action
8. Building capacity to improve health involves the development of sustainable skills, resources, and organizational structures in the affected community
9. Community Empowerment takes place at three levels: the individual, the organization or group, and the community. Empowerment at one level can influence empowerment at the other levels Furthermore, empowerment is multidimensional, taking place in sociological, psychological, economic, political, and other dimensions
10. Community engagement often involves building coalitions, defined as "a union of people and organizations working to influence outcomes on a specific problem." Coalitions can help the engagement process in a number of ways, including maximizing the influence of individuals and organizations, creating new collective resources, and reducing the duplication of efforts The effectiveness of coalitions has been evaluated on two distinct bases: how well the members work together, and what kinds of community-level changes they bring about.
11. Done well, the community-engaged approach can enable partnerships to develop programs and research "in ways that are consistent with a people's and community's cultural framework"

Community Engagement Themes and Activities

The goal of engaging HCWs, communities, and NSAs is to contribute to the achievement of universal health coverage and comprehensive care in TB, Leprosy & lung health. This goal can be realized through various approaches and activities as highlighted in the table below.

Theme	Activities
Prevention	Awareness-raising, information, education & communication, behavior change communication (BCC), infection control, identification & training of providers & TB Champions / Advocates (Multi-sectoral & Multidisciplinary Collaborative Engagement)
Diagnosis	Screening, contact tracing, sputum collection and transportation, provider training
Referral	Linking with clinics/community support systems, transport support and facilitation, accompaniment, referral forms, and training of health providers (Multi-sectoral & Multidisciplinary Collaborative Engagement)
Treatment adherence support	Home-based supervision and patient support, adherence counseling, stigma reduction, pill counting, training of providers, home-based care and support, SMS reminders (Multi-sectoral & Multidisciplinary Collaborative Engagement)
Social and livelihood support (social protection)	Cash transfer, insurance schemes (e.g. NHIF), nutrition support and supplementation, voluntary savings and loans, and inclusive market that extend choices and opportunities to the poor, training of health care providers, income generation (Multi-sectoral & Multidisciplinary collaborative engagement)
Stigma reduction	Community theatres/ drama groups/ testimonies, partner/peer support groups, community champions, sensitizing and training facility and CHVs and community own resource persons (CORPs) (Multi-sectoral & Multidisciplinary collaborative engagement)
Advocacy	Ensuring availability of resources (human, financial, supplies, equipment etc.) and services, training of providers, addressing governance and policies issues, working with community leaders (Multi-sectoral & Multi-disciplinary collaborative Engagement)

The Three Basic Components of TB Programming

(These can be tweaked to apply to leprosy)

1. Finding the people who may have TB and providing access to diagnosis. This is known as case detection. It may be done through symptom screening or contact tracing (tracking down people who have been exposed to someone with TB). Typically, sputum (coughed-up mucus) samples produced by persons presumed to have TB are taken to a laboratory for testing to facilitate a diagnosis. In some places, chest x-rays are also used as part of screening for TB.

2. Ensuring that those who have TB receive a supply of quality-assured medicine, begin treatment, and are able to take the entire course of medicine consistently and completely.

3. Minimizing the spread of TB through prevention and infection control. Health facilities and medical staff alone cannot do all of this work. To reach the goal of eliminating TB in Kenya, more people and organizations need to get involved. We need a wide variety of people, organizations, and groups to engage communities and work together to help stop TB. As a team, we can prevent many people from ever catching or developing active TB in the first place, as well as help those on therapy complete treatment.

The above can apply to Leprosy as well as part of a broad strategy to eradicate Leprosy in Kenya.

A Highlight of the Strategies for the Three Basic Components of TB Programming

A. Steps to Community Case Identification and Diagnosis

1. Create awareness among community members to increase demand for TB, Leprosy, and lung disease services through community outreaches, health talks, health education, and/or prevention campaigns/initiatives
2. Identify persons with signs and symptoms of TB, Leprosy, and lung disease using community screening tool (intensive case finding)
3. Refer and link presumptive TB/leprosy cases to a health facility for further evaluation
4. Collect and/or ship sputum specimen to facilities (*where applicable*)
5. Contact trace (use of facility TB/leprosy data to follow up on contacts of bacteriologically confirmed TB patients; multibacillary leprosy patients)
6. Address / reduce stigma related to the disease

B. Approaches for Patient Care and Support at Community Level

1. Implement a good DOTS program at the community
    1.1. Advice the patient on the availability of community-based patient management options (ambulatory services) for both drug-sensitive and resistant TB and leprosy management
    1.2. Provide DOT for Rifampicin based regimens at the household level
2. Promote the provision of social and livelihood support (social protection for TB, leprosy patients), including but not limited to:
    2.1. Nutrition support
    2.2. Income-generation activities for the aged, orphaned and vulnerable children, etc.
    2.3. Stipends during the treatment period

2.4. Enrollment into NHIF for care support during and after the treatment period

2.5. Reintegrate TB patients into the community post-recovery, e.g., joining/ participating in the community activities

3. Refer/link patients for Psychosocial support (to existing community-based program) providing care and support services including:

3.1. Counseling

3.2. Patient follow up to ensure completion of treatment

3.3. Establish support groups in the community and link patients accordingly

3.4. Home visits by community health volunteers to ensure adherence to medication and nutritional therapy

3.5. Tracing of patients who might interrupt treatment

3.6. Post-treatment support for former patients and their household

4. Link and/or refer to leprosy patients (those with disability grade 1&2) for rehabilitative services (social, surgical, etc).

C. Approaches for Infection Prevention and Control at the Community Level

1. Provide health education for the patient, family and community on how to minimize disease transmission at the household level
2. Ensure timely vaccination for all 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 high coverage.
3. Promote the provision of TPT for children exposed to infectious cases.

Coordination of TB and Leprosy Interventions in the Community

National and County Governments

Engagement with the government and active participation with them is crucial for the successful implementation of TB and Leprosy interventions. Government formulates and oversees policy implementation.

Community-Based Approaches

Community Mapping: A mapping exercise should be conducted every six months to locate administrative boundaries, discern the community's own resource persons, identify the community-based health interventions, including maternal and child health services, available health facilities, services offered, health-seeking behaviors, and

potential barriers to accessing health care services. These will guide in program design and delivery.

Focus Group Discussions: FGDs should be conducted to initiate discussions around the CHV program, address any issues arising from the mapping exercise, and develop a desirable relationship with key community stakeholders in order to secure and sustain the community's interest in all aspects of the program. These consultations should be used to discuss health issues in the community and ask about existing TBAs and health leaders. It is also useful to visit the homes of the TBAs to understand the scope of their work and the homes of community members to learn from whom they already seek health advice and services. Community dialogue can culminate into community action.

Community Face-to-Face Sensitizations: It also helps to manage expectations and prepare the community for new interventions. It is good to share plans with the community prior to the rollout to help them prepare and clarify any questions they may have. CHVs serve as the gatekeepers, and once they are known by the community members, they can be used to prepare the community for any other new interventions.

Community sensitization should meet the following objectives

1. To provide background information about the CHV program.
2. To discuss the health status of the community and the need to improve health outcomes.
3. To respond to and address any concerns that may arise during such community entry activities.
4. To seek community approval for the recruitment of CHVs and their participation in the program.
5. To seek collaboration with partner/referral health facilities and schools in the area of coverage.
6. To identify existing community structures to work with.
7. To hold face to face meetings with local leaders'/opinion leaders.

Establishing criteria that respect equity

Each program needs to develop standards that CHV must meet. CHVs who are from the same community as their clients are uniquely situated to build trusting relationships with their clients. Other qualifications, knowledge, skills, abilities, and experience follow the criteria for the selection of community health volunteers.

Determining Roles and Responsibilities: Each program needs to develop a job description with specific roles, responsibilities, and activities for Community Health Workers. Most job descriptions are specific to program needs, resources, and the service package to be delivered by the CHVs. However, the **engagement of CHVs shall align** with the ministry of health and county and sub-county guidelines.

Some qualities of a CHV

1. Must be of age
2. Preferably a resident of the area or community being served
3. Selected by the community
4. Be committed to the role
5. Be able to read and write
6. A community mobilizer
7. Have knowledge of health issues, system, and development
8. Understand the local language
9. Able to influence people for change
10. Demonstrate conflict resolution skills
11. Be culturally sensitive

Supervision of TB Activities in the Community

Systematic supervision is a necessary part of a successful CHV program. It is imperative that CHVs have clear expectations and are regularly supported and mentored as they fulfill the goals of the CHV program. Effective supervision is known to improve the knowledge and skills of CHVs and the quality of care provided to patients and raise awareness of the CHV role, thus legitimizing CHVs and their work in the eyes of community members. A 360 model of supervision has been suggested as a guide to efficient supervision.

The 360 Supervision Model

The steps in the model are as follows:

1) **CHV Dashboard:** CHV supervisors review the CHV performance data, which tracks speed, quantity, and quality of care.
2) **Patient Feedback Audit:** CHV supervisors conduct home visits to families visited by the CHWs in their absence in order to collect performance feedback.
3) **CHV Shadowing:** CHV supervisors visit households alongside CHVs in order to directly observe the CHV providing care during home visits.
4) **One on One Feedback:** CHV supervisors sit down with their CHVs to collaboratively set goals and identify areas of strength and areas of improvement. They should discuss individual and aggregate performance, logistical challenges, and solutions, and the supervisor should ensure that all CHVs have and know how to use job aids, counseling cards, and smartphones.

Start-up Costs for a CHV Program: Start-up costs may be variable from program to program depending on the design and the service package and can include many components such as planning costs, training costs, CHV Kits, equipment, basic

supplies/consumables, airtime, uniforms, and development of any needed physical infrastructure (e.g., meeting spaces, information technology infrastructure, payroll, and human resources systems.

The Roles of Community Stakeholders in TB, Leprosy & Lung Health Disease Control

Community Health Committee (CHC)

- The coordination and management of the CHU and its workforce shall be done by a
- CHC, a group of members selected by the community. The committee shall include:
- A prescribed number of which not more than two-thirds shall be from the same gender.
- Representation from religious and cultural groups within the context.
- Representation from youth and people with disabilities.

The members must reside in the community they are selected to serve. They will serve a three-year term that is renewable once unless agreed by the community. The CHC shall choose its chairperson and shall have at least one, and at most two, CHVs. If a member of the CHC is selected to be a CHV, they cease to be in the CHC unless representing CHVs. The CHA shall be the technical advisor and secretary to the CHC. The treasurer shall be a CHV. The chairperson shall become a co-opted member of the link health facility committee. The CHC shall be the first organ to be constituted in the establishment of a CHU.

The roles and responsibilities of the CHC shall include:

- Provision of leadership and oversight in the implementation of health and another related community service.
- Preparation and presentation of the CHU annual work-plans and operational plans to the link facility health committee.
- Planning, coordinating, and conducting community dialogue and health action days.
- Working with the link facility to promote facility accountability to the community.
- Holding quarterly consultative meetings with the link facility health facility committee.
- Creating an enabling environment for implementation of community health services.
- Resource mobilization for sustainability.

TB Treatment Supporters (e.g., Peers, family members, friends, etc.)

- Provision of DOT (Directly Observed Treatment) to ensure compliance and adherence of treatment
- Provide psychosocial support, e.g., counseling, etc
- Provide 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
- Alcoholics & Drug users

Community Health Volunteer (CHV)

- Create awareness on TB, Leprosy & Lung Health and available services to the community
- Identify, screen, and refer presumptive TB/leprosy clients to the health facility and follow up on the outcome
- Support patients on treatment and adherence
- Tracing of treatment interrupters and patient contacts
- Refer TB patients on treatment for follow-up sputum smears
- Record and report information using the standard tools
- Identify complications, including adverse drug reactions, and refer as needed
- Participate in periodic review meetings organized by the CHEW
- Promote infection prevention and control interventions at the Household/ community level

  Link patients to support groups

  Perform nutrition assessment e.g., weighing patients, using mid-upper-arm circumference (MUAC), etc., and referring appropriately

Note: *These activities are achieved mainly through home visits, barazas, etc.*

Community Health Assistants/Extension Workers (CHAs/CHEWs)

CHAs/CHEWs are directly in contact with the CHVs/Community Health Committee (CHC). They are the link between the community and the local health facility. Other roles include:

1. Participate in the selection, training, and support of Community Health Volunteers (CHVs) and Community Health Committees (CHCs)

2. Being the secretary to the CHC and the custodian for CHC meeting minutes
3. Plan and build the capacity of CHVs
4. Sensitize the CHVs on side effects monitoring (pharmacovigilance)
5. Monitor the management of TB & leprosy patients in the community
6. Generate and collate data for decision making
7. Link the community and the health facility for action
8. Organize community health activities, including dialogue days and health action days
9. Organize periodic review meetings with the CHVs
10. Organize and conduct school health activities (TB, Leprosy, lung health)
11. Provide support supervision to CHVs
12. Ensure patients are appropriately notified and monitored at the community
13. Receives reports from the CHC / CHV and forward them to the HRIO
14. 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 them to the 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 other lung diseases
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 the 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)

1. Empower communities to participate in matters relating to their own health
2. Mobilize communities to participate in resource mobilization for their livelihood
3. Advocate for budget allocation and mobilize resources for sustainability
4. Influence other stakeholders to embrace TB/ leprosy activities in their routines
5. Support and participate in the implementation of TB, leprosy control activities
6. Promote behavior change through various channels of communication to reduce stigma and discrimination
7. Identify and work with key populations
8. Facilitate implementation of TB Intensive Case Finding (screening, referral, and testing)
9. Support and participate in home-based care activities
10. Promote treatment adherence through peer support groups, education, and individual follow-up
11. Promote the provision of social and livelihood support to TB / leprosy patients (e.g., stipends/ food, income-generation activities for the aged, orphaned and vulnerable children, etc)
12. Promote patients' rights and responsibilities
13. Promote infection prevention and control interventions at the 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.*

Field Processes

A Sample Community Outreach Field Process

1) Courtesy call to the CDH or the nearest CHMT representative by the team lead. The rest of the team may go directly to the screening area.
2) People who have been mobilized are taken through Health Education on TB, and their concerns responded to. The number of people attending the health education forum becomes the denominator for the screening population.
3) Outreach teams assemble and strategically position themselves to facilitate free patient flow.
4) Everyone present is screened by the clinician through the use of the TB screening criteria and their details documented.
5) Anybody responding affirmatively to any of the screening questions is further investigated by the clinician (Presumptive TB Patients).
6) TB presumptive patients are recorded in the presumptive register and may be sent for Chest X-Ray. (NB: chest X-rays will only be done to those with the request form from the clinician).
7) Those with abnormal chest x-ray outcomes are referred for Gene X-pert test.
8) Those who are diagnosed to have TB either through clinical diagnosis or bacteriological confirmation should be put in the TB4 register and initiated on treatment.
    a) Those with normal chest X-ray outcomes are investigated by the clinician for other chest conditions.
    b) Those who test negative for Gene X-pert (MTB-Negative / MTB not detected) are further evaluated and managed accordingly.
    c) Those who test positive for Gene X-pert (MTB-Positive / MTB detected) are initiated on treatment according to the National TB treatment guidelines and recorded in the TB4 register of the nearest health facility.
9) The TB positive patients are then linked to the SCTLC for further follow up, contact tracing, and social support (support groups, NHIF for DRTB patients).

A Sample Process for a Targeted Mobile X-ray Outreach

1) Counties make their request to be supported with the mobile digital X-Ray machine/s to the Head of NTLD-P.
2) Requests from either S/CTLC have to be supported by some justification.

Outreaches target vulnerable populations and those in congregate settings. Some of the key populations targeted include; people who abuse drugs, prison inmates, factory workers, people in learning and training institutions, those living in informal settlements, among others.

3) The Head, NTLD-P, approves, or disapproves the requests based on justification.

4) The Head NTLD-P will source for funding from partners.

5) The team leaves for a field outreach.

Monitoring Community Engagement

WHO has developed a minimum set of standardized indicators to help monitor contributions made by communities (particularly CHVs) whether supported by the government or by partners.

NB: *Utilization of the TB ACF (Active Case Finding) data tools and community outreach data flow charts/SOPs will be highly recommended*

The following are the additional activities on monitoring of community engagement that can be carried out by community health extension workers and community health volunteers:

- Continuous capacity building of CHVs and Champions/advocates from other sectors
- Ensure accurate and orderly record-keeping of community tools
- Ensuring presumptive cases reaching the facility is entered into the presumptive/ contact investigation register (where applicable)
- Emphasize and utilize the "remarks" column in the various tools to indicate referral to/from the community for proper analysis
- Periodically document on the community engagement, multi-sectoral / multi-disciplinary best practices

MONITORING & EVALUATION

20

20.1 Introduction

Monitoring is the routine tracking of service and program performance. It is a continuous process intended to provide information on the extent to which a program is achieving its targets within specified period.

Evaluation 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. This can be achieved by all health workers at all levels utilizing the information collected routinely to improve service delivery with the aim of achieving the set targets.

20.2 Recording and Reporting

Recording and reporting program of data is vital for Monitoring and Evaluation of the Program. Data forms part of the general health information system, which aims to:

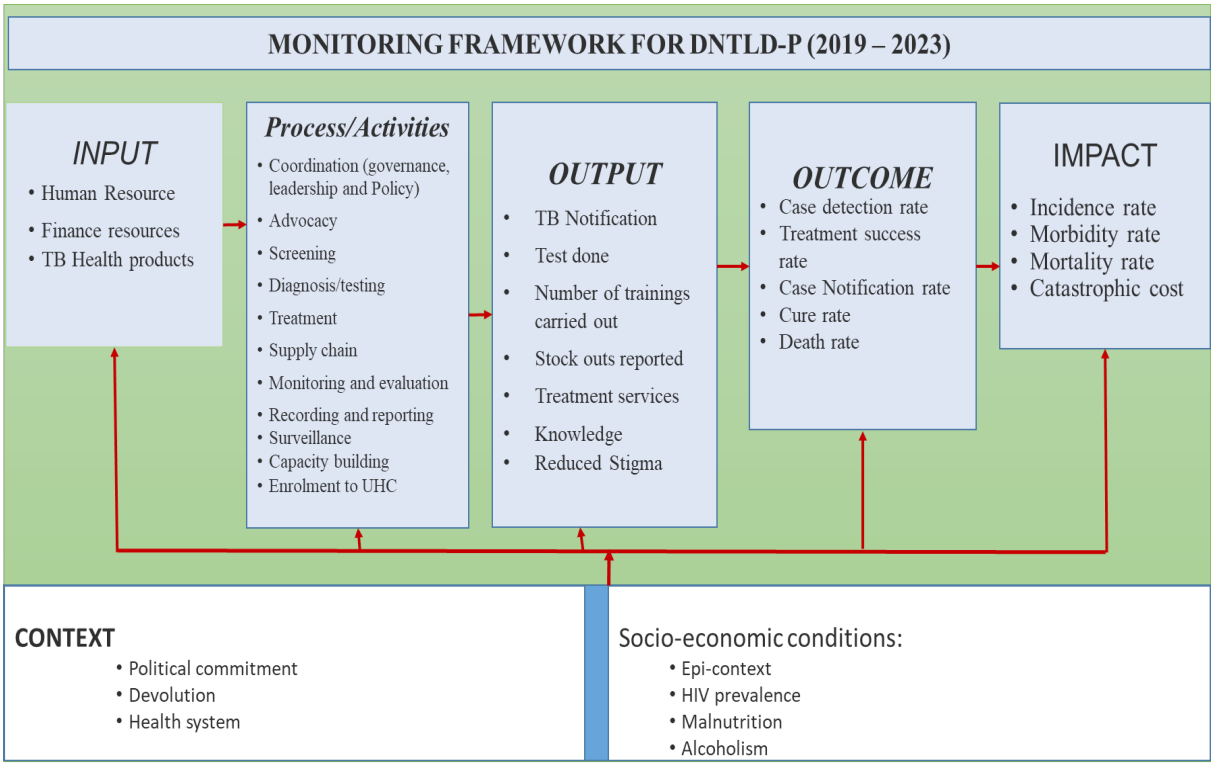
- Ensure a continuum of care, information-sharing with patients and transfer of information between health facilities,
- Enable managers at different levels in the DNTLP to monitor Program performance in a standardized and internationally comparable way, and
- Provide the basis for programmatic and policy development.

Establishment of a reliable recording and reporting system is an essential part of the End TB strategy. These guidelines are accompanied by forms, registers and reporting templates that are designed for paper-based and electronic recording and reporting systems.

- All data collection, storage and use should be in accordance with data protection act of parliament 2019.
- Every health care provider who treats TB has a professional responsibility to record and report all cases he or she treats
- Accurate keeping of records of all individual patients and maintenance of registers are minimum requirements that need to be met by all health care workers involved with the diagnosis and treatment of tuberculosis patients.
- Tuberculosis (TB) case recording and reporting tool is important for monitoring, evaluating and collecting information on each newly reported case of TB disease (TB Surveillance) at either health facility, region, county and nationally.

  Note: TB is a notifiable disease under the Public Health Act Cap 242, and therefore all TB Cases (diagnosed by the public or private sector) must be notified to the MOH.

Figure 20.1 Monitoring and evaluation log framework



20.3 Data Management

Figure 20.2 Data management levels for TB in Kenya

- Facility TB, leprosy and lung disease data may largely be recorded in the standard recording and reporting tools provided by the MOH. While electronic reporting at the facility level is acceptable and encouraged, conformity to the standards provided by the MOH through its reporting framework and health information system policy is mandatory for each electronic tool handling TB, Leprosy and Lung disease data.
- Accurate records of individual patients and maintenance of registers are minimum requirements that need to be met by all healthcare workers involved with the diagnosis and treatment of tuberculosis, leprosy and lung disease patients. It is the responsibility of the facility in charge (I/C) with training and technical support (supervision) from the County and Sub county coordinators to ensure that recording of details about patients is done properly and correctly. The number and design of cards, forms and registers has been limited and kept as simple as possible to enable the DNTLD-P to have good patient care and monitoring of performance at all levels.
- All patients diagnosed in health care facilities supervised by the DNTLD-P must be registered at the start of treatment.

NOTE: TB is a notifiable disease under the Public Health Act Cap 242, and therefore all TB Cases (diagnosed by the public or private sector) must be notified to the MOH

20.4 Archiving & Confidentiality

- The facility is expected to take precautions against fire, other accidents and criminal acts that may affect stored data at the facility. For computer-based records, responsible ICT officers in conjunction with the facility in-charge(s) should ensure proper archiving and accessibility of the data. Because of data sensitivity, appropriate security against unauthorized access and modification should be instituted; particularly where a provider fails to comply with privacy standards prescribed by the health information system policy or any existing or proposed health law or knowingly violates patient privacy. In line with the principles of information privacy, data collected for TB, leprosy and lung diseases by the health workers shall be stored confidentially (lock & key / Password protected). This shall be different from the policies on medical records management.

Care should be exercised to ensure data integrity and data should be safeguarded against unauthorized access and use. Confidentiality should be ensured at all levels and any breech of this should be reported to relevant authorities.

Data analysis and use for decision making at all levels

HCWs at all levels should carry out routine basic data analysis in order to inform management on progress and quality of care provided to the patients. Some of the recommended analysis and quality checks at the facility are:

- Monthly and quarterly trends of TB, leprosy and lung diseases diagnosed and started on treatment
- Treatment outcomes (cohort analysis) per quarter
- AFB microscopy positivity rates for new and follow up tests
- GeneXpert utilization rates
- GeneXpert positivity rates
- GeneXpert error rates
- Proportions of eligible patients done DST
- Proportions of children under 15 years diagnosed with TB.

All operations research activities should be done in line with guidelines from the ethics committees and requirements of NACOSTI adhered to. HCWs are encouraged to utilize readily available data to diagnose any service delivery bottle necks and recommend solutions to the management.

20.5 Roles and Responsibilities

TB is a notifiable disease every health care provider has professional responsibilities to record and report the cases.

County TB and Leprosy coordinator (CTLC)

- Provide oversight of TB, leprosy and lung health programming in county
- Build capacity of SCTLCs and HCWs through micro-teachings, on-job mentorship, facility CMEs and by availing of job aids, SOPs and guidelines
- SCTLC support supervision
- Avail recording and reporting tools

Sub-county TB and Leprosy coordinator (SCTLC):

- Provide oversight of TB programming in sub-county
- Build capacity of HCWs through micro-teachings, on-job mentorship, facility CMEs, and by availing of job aids, SOPs and guidelines
- HCW support supervision
- Avail recording and reporting tools
- Notify all TB patients
- Ensure proper documentation is done

HCW at all SDPs

- Clinical evaluation for TB diagnosis (history taking, physical exam)
- Makes Lab requests and refer TB cases for GeneXpert/ smear microscopy (CXR as appropriate)
- Interpret lab results and make a diagnosis as appropriate.
- Start treatment initiation and contact management
- Monitor side effects, record and report
- Documentation in the appointment cards, record cards and TB registers

Laboratory personnel

- Carry out Laboratory investigation and relay results back to the referring clinicians
- Follow up confirmed TB patients on diagnosis to return for treatment initiation
- Documentation of lab request form and registers

Table 20.1 Data collection tools for TB in Kenya

No	Name of Tool	Purpose	Location	Filled By
1	Tuberculosis screening/Contact tracing form at community level	It is an ICF cards Used for screening TB in the community	Community	CHV
2	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
3	Patient Appointment Diary	Used to record clinic appointment details for patients on TB treatment	TB clinic	Clinician
4	Treatment Interruption Tracing Form for Community Health Volunteers	Used to track patients who have defaulted TB treatment.	Facility	CHV
5	Facility Summary Tool for Facility-Based Active Case Finding	This is a summary tool used to record summary ACF data in a facility from all the departments per month	Facility	Clinician
6	Departmental Summary Tool for Facility -Based Active Case Finding	This is a summary tool used to record summary ACF data per department per month	Facility	Clinician
7	MDR Lab Investigation Request Form	This is a form used to request for further lab investigation for a DR-TB patient before and during the treatment course	Facility	Clinicians
8	AFB/GeneXpert / Culture Register	It is a case listing for all pulmonary TB patients sent for AFB microscopy and gene xpert tests done in the lab.	Lab	Lab officers
9	EQA Analysis Form	This is used to record the EQA results by the lab	Lab	Lab officers
10	EQA Summary Form	Used to collect microscopy EQA performance by the Lab coordinator	Lab	Lab officers
11	Laboratory Support Supervision Checklist	It is a duplicated checklist booklet used by the lab coordinator to conduct supervision to the facilities doing smear microscopy	Lab	Lab officers
12	Workload Summary Form	Used to collect monthly laboratory data for microscopy, Xpert data, Culture data	Lab	Lab officers

No	Name of Tool	Purpose	Location	Filled By
13	EQA Sampling Sheet	Used by the TB coordinator to sample slides for EQA controls	Lab	TB Coordinator
14	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
15	Asthma Register	It is Asthma Case listing register which summarizes key variables for tracking Asthma patient progress.	Outpatient/ Chest Clinic	Clinicians
16	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	Clinicians
17	Patient Appointment Card (TB, TPT, DRTB, Leprosy and Asthma)	The card is used for scheduling treatment appointments and acts as a treatment reminder to the patient.	Patient	Clinicians
18	Bin Card	This card is used to monitor stock of commodities in facility store or pharmacy	Pharmacy/ Store	Pharmacist
19	S11	This form is in triplicate and is used to issue out commodities to various service delivery points within the facility	Pharmacy/ Store	Pharmacist
20	Intensive Case Finding /TPT Card	This form is used both for screening for TB among the at-risk population (both adults and children) and recording TPT information for eligible patients	TB, and HIV clinic	Clinicians
21	TPT/Contact Management Register	It is a Case listing which summarizes key variables for listing and management of contacts of bacteriologically confirmed PTB and TPT patient progress and outcomes.	TB and HIV clinic	Clinicians
22	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
23	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

No	Name of Tool	Purpose	Location	Filled By
24	Culture/DST Log book	To capture patients whose samples have been sent for culture and DST and results	TB clinic	Clinicians
25	AFB/GeneXpert/ Culture request form	Used to request for AFB/Gene xpert/culture/DST for DR TB surveillance	TB Clinic	Clinicians
26	DR TB Patient Log book	Individual patient management booklet that records all information regarding the patient.	TB clinic	Clinicians
29	DR TB Register	DRTB Case listing which summarizes key variables for tracking patient progress and outcomes	TB clinic	Clinicians
30	DR TB baseline and follow up test request form	Baseline and follow-up request form for DR TB patient.	TB clinic	Clinicians
31	Pharmacovigilance Reporting Tools (Yellow)	Reporting a Suspected Adverse Drug Reaction	TB Clinic	Clinicians
32	Pharmacovigilance Reporting Tools (Pink)	Reporting a Suspected Poor-Quality Medicinal Product	Pharmacy/ Store	Pharmacist
33	Pharmacovigilance alert card (White)	The card given to patient who developed ADR	Patient	Clinicians
34	Leprosy record card	The card is filled by health worker and acts as patient clinical record card	TB Clinic	Clinicians
35	Leprosy register	It is a leprosy case listing which summarizes key variables for tracking TB patient progress and outcomes	TB Clinic	Clinicians
36	Monthly Data Chart	It's a monthly summary chart that shows facility performance in various indicators	TB Clinic	Clinicians
37	Facility Referral/ Transfer form for Drug Resistant (DR TB)	This a form used to refer a drug resistant TB patient from one facility to another	TB Clinic	Clinicians
38	Facility Referral/ Transfer form for Drug Sensitive (DS TB)	This a form used to refer a drug sensitive TB patient from one facility to another	TB Clinic	Clinicians
39	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	Clinicians

No	Name of Tool	Purpose	Location	Filled By
40	Patient referral form from TB clinic.	Used for referring patients for management of other conditions than TB	TB clinic.	Clinicians
41	Facility Daily Activity Drug Register	To monitor the use of the TB and DR-TB drugs on a daily basis	TB clinic/ Pharmacy	Clinician
42	FCDRR	It's a reporting tool for consumption of TB, and DR TB drugs	TB clinic/ Pharmacy	Pharma-cist/ Clinician

Table 20.2 Indicator definition, measurement

Below are some of the indicators which can be tracked at the service level.

Indicator	Indicator definition	Frequency	Source of data
Drug susceptible TB			
Proportion of pre-sumptive TB cases (with respiratory symptoms) with lab-oratory investigation for TB	**Numerator:** Number of presumptive TB cases tested **Denominator:** Total number of people pre-sumed to have TB	Quarterly	TIBU/Pre-sumptive Register/KHIS
Number of people notified with TB (all forms)	Number of DSTB people (all forms) notified	Quarterly	TIBU
Case notification rate (CNR)	**Numerator:** Number of people notified with TB (all forms) **Denominator:** Total projected population of a county per year	Yearly	TIBU/KNBS
Sputum conversion rate at the end of intensive phase	**Numerator:** No. of bacteriologically con-firmed cases with a negative smear result at the end of the intensive phase **Denominator:** Total number of bacteriologi-cally confirmed cases started on treatment	Quarterly	TIBU
Proportion of noti-fied TB cases eval-uated for nutritional support	**Numerator:** Number of notified TB cases with nutritional assessment **Denominator:** Total number of notified TB cases	Annual	Annual report
Proportion of eligi-ble malnourished TB cases who re-ceived appropriate nutrition support	**Numerator:** Number of malnourished (Se-vere and Moderate) patients offered appro-priate nutritional support **Denominator:** Total number of assessed TB cases who required nutritional support	Annual	Annual report

Indicator	Indicator definition	Frequency	Source of data
Mortality rate among malnourished TB patients	**Numerator:** Number of deaths among notified TB cases who are malnourished **Denominator:** Total number of notified malnourished TB cases	Annual	Annual report
Treatment success rate (all forms); Percentage of TB cases successfully treated	**Numerator:** Total number of patients with outcomes cured and treatment completed **Denominator:** Total number of patients notified	Quarterly	TIBU
Cure rate for bacteriologically confirmed pulmonary TB cases (both New and Relapse)	**Numerator:** No. of bacteriologically confirmed PTB cases with a cure outcome at the end of treatment **Denominator:** Total number of bacteriologically confirmed PTB cases notified	Quarterly	TIBU
TB death rate (All forms of TB)	**Numerator:** Total number of TB patients with Died outcome in the register **Denominator:** Total number of patients notified	Annual	TIBU
Lost to follow-up (All forms of TB)	**Numerator:** Total number of TB patients with a lost to follow-up outcome in the register **Denominator:** Total number of patients notified	Annual	TIBU
Programmatic Management of Drug Resistance TB			
Proportion of notified TB patients who receive DST	**Numerator:** No. of notified TB cases tested with a WRD as the initial Diagnostic test **Denominator:** Total number of notified TB cases	Quarterly	TIBU
Number of TB cases with Rifampicin-resistant TB (RR-TB) and/or MDR-TB notified	Number of TB cases with RR-TB and/or MDR-TB notified to the National TB program	Quarterly	TIBU/ TB4/ DRTB register
Number of cases with RR-TB and/or MDR-TB that began second-line treatment	Number of cases with RR-TB and/or MDR-TB that began second-line treatment	Quarterly	TIBU/DRTB register
Treatment success rate; Percentage of DRTB cases successfully treated	**Numerator:** Total number of DRTB patients with outcomes cured and treatment completed **Denominator:** Total number of DRTB patients notified	Quarterly	TIBU

Indicator	Indicator definition	Frequency	Source of data
Childhood TB			
Proportion of children with TB among notified TB Patients	**Numerator:** Number of notified children (<15 years) with TB **Denominator:** Total number of notified TB cases	Quarterly	TIBU
Pediatric TB treatment success rate	**Numerator:** Number of pediatric TB cases who cured or completed treatment **Denominator:** Total number of notified pediatric TB cases	Quarterly	TIBU
Proportion (%) of children under 5 household contacts put on TPT	**Numerator:** Total number of under 5 children household contacts put on TPT. **Denominator:** Total number of children under 5 household contacts who are eligible for TPT	Quarterly	TIBU
Proportion (%) of household contacts over 5 put on TPT	**Numerator:** Total number of household contacts 5+ years old put on TPT. **Denominator:** Total number of household contacs 5+ years old who are eligible for TPT	Quarterly	TIBU
Active Case Finding			
Number screened for TB	**Numerator:** number of people who are presumptive **Denominator:** Total number of patients visited health facility	Monthly	OPD registers (MOH 204)
Number of presumptive cases	**Numerator:** Number of people screened for TB **Denominator:** Total number of patients screened for TB	Monthly	OPD registers (MOH 204)
Number of presumptive TB cases investigated for TB	**Numerator:** number of people with presumptive cases investigated for TB **Denominator:** Total number of patients screened for TB	Monthly	presumptive register/TIBU
Number bacteriologically confirmed with TB	**Numerator:** number of cases bacteriologically confirmed **Denominator:** Total number of presumptive cases investigated for TB	Monthly	presumptive register/TIBU
Number clinically diagnosed with TB	**Numerator:** number clinically diagnosed with TB **Denominator:** Total number of presumptive TB cases investigated	Monthly	presumptive register/TIBU

Indicator	Indicator definition	Frequency	Source of data
TB/HIV			
Proportion of registered TB patients (all forms) with documented HIV status	**Numerator:** number of TB patients with documented HIV status (Positive and Negative) **Denominator:** Total number of notified TB patients	Quarterly	TIBU
Proportion of HIV - positive TB patients started on ART	**Numerator:** number of HIV positive TB patients started on ART **Denominator:** Total number of notified TB patients who were HIV Positive	Quarterly	TIBU
Treatment success rate among HIV-positive TB cases	**Numerator:** Number of notified HIV positive TB cases who got cured or completed treatment **Denominator:** Total number of notified HIV positive TB cases	Quarterly	TIBU
Proportion of PLHIV initiated on TB Preventive Therapy	**Numerator:** Number of PLHIV initiated on TB Preventive Therapy **Denominator:** Total number of PLHIV on care	Quarterly	MOH731/ KHIS
Proportion (%) of PLHIV initiated on TPT who have completed a course of TPT	**Numerator**: Total number of PLHIV initiated on TPT 6 months before who successfully completed TPT during the reporting period **Denominator**: Total number of PLHIV initiated on TPT 6 months before.		
Public Private Mix			
Proportion of notified TB cases (all forms) contributed by non-national TB program providers – private/non-governmental facilities	**Numerator:** Number of TB cases (all forms) that are notified by private health facilities to the National TB Program **Denominator:** Number of TB cases (all forms) notified to the National TB Program	Quarterly Yearly	TIBU
Number of counties engaging the informal sector providers in TB care and prevention	Number of counties engaging the informal sector providers in TB care and prevention	Annual	ISP providers reports
Proportions of people with TB referred by private/NGO facilities	**Numerator**: Number of people with TB referred by private/NGO facilities **Denominator**: Total number of people with TB notified	Quarterly	TIBU/ Facility registers

Indicator	Indicator definition	Frequency	Source of data
Human Rights and Gender			
Number of lawmakers, law enforcement agents and HCWs sensitized on human rights and gender	Number of lawmakers, law enforcement agents and HCW sensitized on human rights and gender by the TB program and other partners.	Annual	Annual reports
Proportion of people with TB reached with legal literacy (know your rights) campaigns to improve legal and human rights literacy	**Numerator:** Number of patients with TB reached legal literacy (know your rights) campaigns to improve legal and human rights literacy **Denominator:** Number of TB patients notified	Annually	Annual reports
Number of Government/legal stakeholders (Ministries, national human rights institutions, Gender Commission and Office of the Ombudsmen) sensitized on human rights dimensions of TB, leprosy and lung diseases.	Number of Government/legal stakeholders sensitized on human rights dimensions of TB, leprosy and lung diseases.	Annualy	Annual reports
Number of people who face human right violations provided with TB, leprosy and lung diseases related legal services	Number of TB, Leprosy and lung disease patients who received disease related legal services	Yearly	Reports
Supply Chain & aDSM			
Reporting rates for central stores on TB medicine	**Numerator;** Number of TB central stores reporting on TB medicine **Denominator;** Total number of TB central stores	Monthly	TB Allocation tool
Reporting rates for central stores on laboratory commodities	**Numerator;** Number of TB diagnostic sites reporting on lab commodities **Denominator:** Total number of TB diagnostic sites	Monthly	TB Allocation tool

Indicator	Indicator definition	Frequency	Source of data
Number of ADRs reported to PPB	Number of ADR cases notified to the PPB	Quarterly	PPB
Proportion of counties stocking Lung Health commodities	**Numerator:** Number of counties stocking PAL commodities **Denominator:** Total number of Counties	Bi-annual	Report
Proportion of Lung Health essential drugs in the Essential list	**Numerator:** Number of PAL essential drugs in the Essential list **Denominator:** Total number of PAL Essential drugs	Bi-annual	Report
Proportion of health facilities with the minimum Lung Health equipment	**Numerator:** Number of health facilities with the minimum PAL equipment **Denominator:** Total number of facilities	Bi-annual	Report
Leprosy			
Proportion of notified leprosy patients with disability grade 2	**Numerator:** Number of notified leprosy cases with disability grade 2 **Denominator:** Total number of notified leprosy cases	Annual	TIBU
Proportion of notified leprosy cases who are children	**Numerator:** Number of notified childhood (< 15 years) leprosy cases **Denominator:** Total number of notified leprosy cases	Annual	TIBU
Diagnostics			
EQA Coverage (Laboratories)	**Numerator:** Number of laboratories enrolled in EQA **Denominator:** Total number of laboratories	Quarterly	EQA Workbook
Unsatisfactory EQA (laboratories)	**Numerator:** Total number of labs with un acceptable performance **Denominator: T**otal number of labs participating in EQA	EQA feedback form	Quarterly reports
Proportion of Gene Xpert sites enrolled in EQA	**Numerator:** Total number of gene xpert sites enrolled for EQA **Denominator: T**otal number of gene xpert sites	EQA feedback form	Quarterly reports
Gene Xpert utilization Rate	**Numerator:** Total Number of test done per machine **Denominator:** Total number of test expected based on machine modules capacity	AFB/Gene xpert register/LIMS	Quarterly reports
Gene Xpert positivity rate	**Numerator:** Number of positive test results **Denominator:** Total test done using Gene xpert	AFB/Gene xpert register/LIMS	Quarterly reports

Indicator	Indicator definition	Frequency	Source of data
Gene Xpert error rate	**Numerator:** Total Number of errors recorded **Denominator:** Total test done using Gene xpert	AFB/Gene xpert register/LIMS	Quarterly reports
Community TB			
Proportion of bacteriologically confirmed PTB patients and children under 5 reached for household contact tracing	**Numerator:** Number of bacteriologically confirmed PTB patients and children under 5 visited for contact tracing **Denominator:** Total number of bacteriologically confirmed PTB cases and children under 5	Quarterly	TIBU/Contact management register
Proportion of contacts of bacteriologically confirmed PTB cases traced and screened for TB	**Numerator:** Number of contacts of bacteriologically confirmed PTB cases traced and screened for TB **Denominator:** Total number of contacts of bacteriologically confirmed PTB cases	Quarterly	TIBU/Contact management register
Proportion of people with TB referred by community health volunteers and Informal Service Providers	**Numerator:** Number of people with TB refered by CHVs and ISP **Denominator:** Total number of DSTB patients all forms	Quarterly	TIBU
Number of of community actors (Civil society organizations (CSOs), community based organizations (CBOs), community health volunteers (CHVs), community health extension workers (CHEWs), religious leaders and other community leaders) capacity built on community TB through various mechanisms	Number of community actors capacity built on community TB segregated by type	Quarterly	Quarterly reports
Number of outreaches targeting Key population for TB in the community	Number of outreaches targeting Key population for TB in the community	Quarterly	Quarterly reports

Indicator	Indicator definition	Frequency	Source of data
Number of key populations screened for TB in the community through outreaches	Number of key populations screened for TB in the community through outreaches	Quarterly	Quarterly reports
Lung Health			
Number of patients screened for Asthma	This indicator provides an absolute number of patients screened for Asthma in a particular month	Monthly	Asthma register/OPD Register
Number of healthcare workers trained on Lung health	Number of healthcare workers trained on Lung health	Quarterly	Training Database
Proportion of PTB patients screened for PTLD	**Numerator**: No of PTB patients screened for PTLD **Denominator**: Total no of PTB patients started on treatment.	Quarterly	TB register
Proportion of PTB patients diagnosed with PTLD	**Numerator:** No of PTB patients diagnosed with PTLD **Denominator**: No of PTB patients screened	Quarterly	TB register
Proportion of PTB patients diagnosed with COPD	**Numerator**: No of PTB patients diagnosed with COPD **Denominator:** No of PTB patients screened	Quarterly	TB register

ANNEXES

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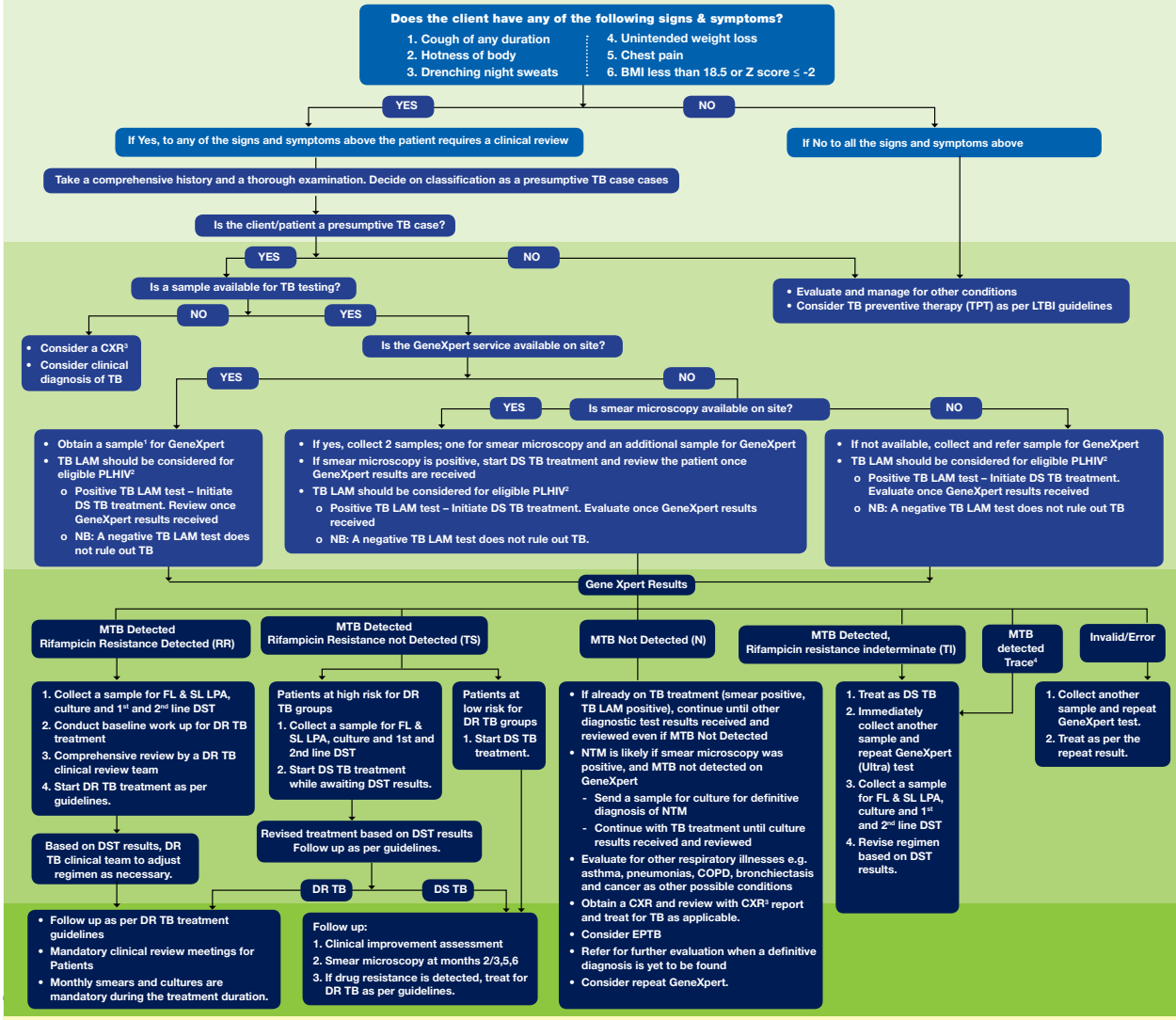
Annex 2: TB Diagnostic Algorithm (Adults)

REPUBLIC OF KENYA

MINISTRY OF HEALTH

TB SCREENING AND DIAGNOSTIC ALGORITHM FOR CHILDREN ≥10yrs AND ADULTS

GeneXpert is the recommended initial test for TB diagnosis. However, where a facility has no GeneXpert, smear microscopy SHOULD BE USED as another sample is collected & referred for GeneXpert.
TB LAM should be used where indicated among PLHIV as per guidelines. TB LAM SHOULD NOT be used as an alternative to GeneXpert testing.



Footnotes

1 Samples for GeneXpert - sputum, CSF, Pleural aspirate, Peritoneal fluid, synovial fluid, Gastric Aspirate, Nasopharyngeal aspirate, FNA, Lymph node biopsy, Pus, stool

2 Indications for use of TB-LAM, as an adjunct test to GeneXpert:
- PLHIV with advanced disease (WHO stage 3 or 4 or CD4 count ≤200 cells/mm³ (or ≤25% for children ≤5years old) with presumed TB
- PLHIV that have any danger signs of severe illness: respiratory rate >30 breaths per minute, temperature >39°C, heart rate >120 beats per minute, unable to walk unaided
- Currently admitted to hospital

3 All CHEST X-rays should be reported and the reports reviewed by the clinician for definitive management. Refer to the CXR algorithm for TB diagnosis

4 MTB detected Trace – Results from sample with few bacilli (paucibacillary TB). Rifampicin resistance status.

HIV Testing, using the HTS algorithm 1, is recommended during TB screening and diagnosis.

Screening for diabetes is recommended among all adult patients with TB disease

Key

CXR	Chest X-ray	LPA	Line Probe Assay
DR TB	Drug Resistant TB	MTB	Mycobacteria Tuberculosis
DS TB	Drug Susceptible TB	NTM	Non-Tuberculous Mycobacteria
DST	Drug Susceptibility Testing	TST	Tuberculin skin test
EPTB	Extra pulmonary TB	SL	Second line
FL	First line		

DR TB risk classification among patients

High risk for DR TB*

1. All previously treated TB patients: treatment failures, relapses, treatment after loss to follow up
2. Contacts of Drug Resistant TB patients
3. TB patients with a positive smear result at month 2 or month 5 of TB treatment
4. Patient who develops TB symptoms while on IPT or has had previous IPT exposure
5. Healthcare Workers with TB symptoms
6. Prisoners with TB symptoms
7. Refugees with TB symptoms

Low risk for DR TB

All presumptive TB cases who are **NOT** in the high risk group

***ALL** the high risk patients **MUST** be prioritized to receive DST - Genexpert, FL and SL LPA, culture and FL and SL DST.

DS TB follow up and DR TB surveillance

POSITIVE SMEAR RESULT AT	Action
Month 2/3	• Evaluate for **adherence**, and other causes of **delayed conversion** • Request for **all** the following **drug susceptibility tests** (DST); GeneXpert, FL LPA and SL LPA. Culture and FL and SL DST • **Continue with RHZE** for one more month, or longer if DST results not received by then • Adjust treatment regimen based on DST results • Repeat smear microscopy at end of month 3. If smear positive continue with RHZE and review DST results and inform the SCTLC immediately • Do not proceed to the continuation phase (RH) without a DST result confirming susceptibility to RH (rifampicin and isoniazid)
Month 5 or month 6	• **Declare treatment failure** and stop anti-TB treatment • Review by the sub county and county TB clinical review teams • Evaluate for adherence, other causes of delayed conversion and treatment failure • Request for GeneXpert, FL LPA and SL LPA, Culture and FL and SL DST • Review DST results and re-initiate treatment based on DST results and other clinical findings
DR TB follow up and DR TB surveillance	
Smear positive or culture positive at month 3 or later	• Evaluate for **adherence**, and other causes of **delayed conversion** • Request for the following **drug susceptibility tests** (DST) (GeneXpert, Culture and First Line (FL) and SL DST, FL LPA and SL LPA) depending on the initial resistance pattern o Review by the sub county and county clinical review teams ▪ Evaluate for adherence, other causes of reversion and treatment failure ▪ Review the DST results o Declare failure if at the end of the extended intensive phase (refer to DR TB guidelines) o Send a case summary to the national clinical team after review by the county clinical team • Do not proceed to the continuation phase (depending on treatment regimen) without a DST result
Smear positive smears and/or cultures during continuation phase	• Declare treatment failure o Review by the sub county and county clinical review teams ▪ Evaluate for adherence, other causes of reversion and treatment failure ▪ Review the DST results • Send a case summary to the national clinical team after review by the county clinical team

MOH/DNTLDP/TBSDXALG/01
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Annex 3: TB Diagnostic Algorithm (Children)

REPUBLIC OF KENYA

MINISTRY OF HEALTH

ALGORITHM FOR PULMONARY TB DIAGNOSIS IN CHILDREN

History of presenting illness	For all children presenting to a health facility ask for the following suggestive symptoms: • **Cough,** • **fever,** • **poor weight gain,** • **lethargy or reduced playfulness** Suspect TB if the child has **two or more** of these suggestive symptoms. Ask for history of contact with adult/adolescent with chronic cough or TB within the last 2 years	
Clinical evaluation	Examine the child and check for: • Temperature > 37.5 (fever) • Weight (to confirm poor weight gain, weight loss) - check growth monitoring curve) • Respiratory rate (fast breathing) • Respiratory system examination – any abnormal findings Examine other systems for abnormal signs suggestive of extra-pulmonary TB#	
Investigations	Obtain specimen* for Xpert MTB/RIF (and culture when indicated**) Do a chest Xray (where available) Do a Mantoux test***(Where available) Do a HIV test DO other tests to diagnose extra-pulmonary TB where suspected#	
Diagnosis	**Bacteriologically confirmed TB:** Diagnose if specimen is positive for MTB	Clinical Diagnosis of PTB: *Child has two or more of the following suggestive symptoms:* • Persistent cough, fever, poor weight gain, lethargy **PLUS two or more of the following:** • Positive contact, abnormal respiratory signs, abnormalnCXR, positive Mantoux **Note:** If the child has clinical signs suggestive of EPTB, refer to EPTB diagnostic table#
Treatment	Treat for TB as follows: • All children with **bacteriologically confirmed TB** • All children with **a clinical diagnosis of TB** NB: In children who do not have an Xpert result, or their Xpert result is negative, but they have clinical signs and symptoms suggestive of TB they should be treated for TB All forms of TB (Except TB meningitis, bone and joint TB): **Treat for 6 months (2 RHZE / 4 RH)** TB meningitis, bone and joint TB: **Treat for 12 months (3RHZE/ 10RH)**	

*Specimen may include: Expectorated sputum (child > 5 years), induced sputum, nasopharyngeal aspirate and gastric aspirate. **Attempt to obtain specimen in every child**

**Do a culture and DST for the following children:
1. Rifampicin resistance detected by the Xpert test
2. Refugees and children in contact with anyone who has Drug Resistant TB
3. Those not responding to TB treatment
4. Those with Indeterminate Xpert results

*** This may include IGRA in facilities where it is available
#Use IMCI guidelines to classify severity of disease
 # Refer to the table on diagnosis of Extra-pulmonary TB

MOH/DNTLDP/CPTBDXALG/01
September 2020

Annex 4: CAGE and CAGE AID Scoring Introduction and Scoring Sheet (Alcohol Abuse)

CAGE and CAGE-AID Introduction and Scoring

The CAGE questionnaire is used to test for alcohol abuse and dependence in adults. The CAGE-AID version of the tool has been adapted to include drug use. These tools are not used to diagnose diseases, but only to indicate whether a problem might exist. The questions are most effective when used as part of a general health history and should NOT be preceded by questions about how much or how frequently the patient drinks or uses drugs. The reason for this is that denial is very common among persons abusing alcohol or other drugs; and therefore, the CAGE/CAGE-AID questions focus the discussion toward the behavioral effects of the drinking or drug use rather than toward the number of drinks or drugs used per day.

Item responses on the CAGE and CAGE-AID are scored 0 or 1, with a higher score indicating alcohol or drug use problems. A total score of 2 or greater is considered clinically significant, which then should lead the physician to ask more specific questions about frequency and quantity.

The downside of the CAGE/CAGE-AID approach is that questions do not discriminate well between active and inactive drinkers or drug users, so following positive scores on the CAGE with questions regarding usual consumption patterns (e.g., frequency/quantity/heaviest consumption) will help make this distinction.

Screening Tools

CAGE

1. Have you ever felt you should **cut down** on your drinking?
2. Have people **annoyed** you by criticizing your drinking?
3. Have you ever felt bad or **guilty** about your drinking?
4. **Eye Opener**: Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover?

Scoring: Item responses on the CAGE are scored 0 for "no" and 1 for "yes" answers. A higher score is an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

CAGE-AID (CAGE Questions Adapted to Include Drugs)

1. Have you ever felt you ought to cut down on your drinking or drug use?
2. Have people annoyed you by criticizing your drinking or drug use?
3. Have you felt bad or guilty about your drinking or drug use?
4. Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover?

Scoring: Item responses on the CAGE-AID are scored 0 for "no" and 1 for "yes" answers. A higher score is an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

Used / reprinted with permission from Brown, R.L., and Rounds, L.A. Conjoint screening questionnaires for alcohol and drug abuse. Wisconsin Medical Journal 94:135-140, 1995.

Annex 5: CAGE-AID Alcohol Abuse Screening Questionnaire

CAGE-AID Questionnaire

Patient Name _____ Date of Visit _____

When thinking about drug use, include illegal drug use and the use of prescription drug other than prescribed.

Questions:	**YES**	**NO**
1. Have you ever felt that you ought to cut down on your drinking or drug use?	☐	☐
2. Have people annoyed you by criticizing your drinking or drug use?	☐	☐
3. Have you ever felt bad or guilty about your drinking or drug use?	☐	☐
4. Have you ever had a drink or used drugs first thing in the morning **to steady your nerves or to get rid of a hangover?**	☐	☐

Scoring
Regard one or more positive responses to the CAGE-AID as a positive screen.

Psychometric Properties

The CAGE-AID exhibited:	**Sensitivity**	**Specificity**
One or more **Yes** responses	0.79	0.77
Two or more **Yes** responses	0.70	0.85

(Brown 1995)

Annex 6: CRAFFT Screening Tool for Adolescent Substance Abuse

CRAFFT Screening Tool for Adolescent Substance Abuse

The following questions concern information about your potential involvement with alcohol and other drugs during the past 12 months. Carefully read each question and decide if your answer is "YES" or "NO". Then mark in the appropriate box beside the question. Please answer every question. If you cannot decide, then choose the response that is mostly right.

When the word "drug" is used, it refers to the use of prescribed or over-the-counter drugs that are used in excess of the directions and any non-medical use of drugs. The various classes of drugs may include but are not limited to: cannabis (e.g., marijuana, hash), solvents (e.g., gas, paints etc…), tranquilizers (e.g., Valium), barbiturates, cocaine, and stimulants (e.g., speed), hallucinogens (e.g., LSD) or narcotics (e.g., Heroin, Oxycontin).

Part A: During the PAST 12 MONTHS, did you:		No	Yes
1.	Drink any alcohol (more than a few sips)? (Do not count sips of alcohol taken during family or religious events.)		
2.	Smoke any marijuana or hashish?		
3.	Use anything else to get high? ("anything else" includes illegal drugs, over the counter and prescription drugs, and things that you sniff or "huff")		
Part B: CRAFFT		No	Yes
1.	Have you ever ridden in a **CAR** driven by someone (including yourself) who was "high" or had been using alcohol or drugs?		
2.	Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?		
3.	Do you ever use alcohol or drugs while you are by yourself, or **ALONE**?		
4.	Do you ever **FORGET** things you did while using alcohol or drugs?		
5.	Do your **FAMILY or FRIENDS** ever tell you that you should cut down on your drinking or drug use?		
6.	Have you ever gotten into **TROUBLE** while you were using alcohol or drugs?		

Annex 7: CRAFFT Screening Tool: Scoring and Interpretation

CRAFFT Screening Tool for Adolescent Substance Abuse

Scoring and Interpretation:

Part A: If "yes" to any questions in Part A, ask all 6 CRAFFT questions. If "no" ask CAR question then stop.

Part B: Score 1 point for each "YES" answer.

CRAFFT Score	Degree of problem related to alcohol or other substance abuse	Suggested Action
0-1	No problems reported	None at this time.
2+	Potential of a significant problem.	Assessment required.

References:

- Knight JR, et al. A new brief screen for adolescent substance abuse. Arch Pediatr Adolesc Med. 1999 Jun;153(6):591-6. PMID: 10357299
- Dhalla S, et al. A review of the psychometric properties of the CRAFFT instrument: 1999-2010. Curr Drug Abuse Rev. 2011 Mar 1;4(1):57-64. PMID: 21466499

Annex 8: PHQ-9 Questionnaire

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

Over the last *2 weeks*, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
		add columns	+	+

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all _____ Somewhat difficult _____ Very difficult _____ Extremely difficult _____

A2663B 10-04-2005

Annex 9: PHQ-9 Patient Depression Scoring tool

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.
Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

A2662B 10-04-2005

Annex 10: Immune Reconstitution Inflammatory Syndrome (IRIS)

Immune Reconstitution Inflammatory Syndrome (IRIS)

Definition:

IRIS is a paradoxical inflammatory reaction against a foreign antigen (alive or dead) in patients who have started ART with reconstitution (improved functioning) of their immune system. The immune system, once it regains some function, is now able to respond against the foreign antigen.

Classification:

- **Unmasked IRIS:** appearance of a previously undiagnosed opportunistic infection (OI) following ART initiation (or switch of ART to a suppressive regimen)
- **Paradoxical IRIS:** worsening of a previously diagnosed disease after ART initiation (or switch of ART to a suppressive regimen)

Risk Factors for IRIS:

- 10-20% of patients who start ART with advanced immunosuppression (refer to section 3) experience clinical deterioration during the first few months due to IRIS
- High risk patients include:
  - Advanced immunosuppression (WHO Stage 3 or 4, or CD4 count ≤ 200 cell/mm3 (or CD4% ≤ 25% for children ≤ 5 years old))
  - Patients with a diagnosed opportunistic infection like TB, MAC, CMV, and PCP
  - Low baseline CD4 (CD4 count ≤ 50 cell/mm^3 or CD4% ≤ 10%)
  - High baseline viral load
  - Substantial increase is CD4 count and drop in viral load after starting ART

Diagnosis of IRIS

- IRIS should be suspected any time a patient has clinical deterioration weeks to months after starting ART (or switching to a suppressive ART regimen)
- Clinical deterioration usually occurs within 4-8 weeks of initiation or change of ART (but can be months afterwards)
- IRIS has varied clinical presentations due to multiple possible pathogens that the immune system may be reacting to, and various immune system reactions; there are generally clinical manifestations consistent with an inflammatory condition
- A high level of suspicion is required when making a diagnosis of IRIS, which is generally one of exclusion
- Rule out the possibility of drug reaction, patient non-adherence to OI treatment, persistently active infection and/or drug resistance to OI treatment
- There could be localized tissue inflammation with or without systemic inflammatory response

Patient evaluation:

In addition to the clinical evaluation for PLHIV outlined in Table 3.1, emphasis should be placed on the following areas during the patient evaluation:

History:

Symptoms and current ARV history:

- Specific systemic symptomatology
- Date of ARV initiation
- Regimen
- Reason for substitution / switch from previous ART if not first line
- Adherence to ART and other ongoing treatment
- HIV viral load
- CD4 count

Prior History:	History of treatment of opportunistic infections:
• ARV toxicity • Drug-drug interaction • CD4 count • HIV viral load	• Date of initiation of treatment • Duration of therapy • Clinical response to treatment • Adherence to the OI treatment • Any default to treatment • Resistance to treatment

Physical Examination:

Vital signs assessment: Temperature, Heart Rate, Blood Pressure, Respiratory rate
Conduct a detailed systemic examination: • Emphasis should be placed on the system(s) which are primarily affected (Table 3.1)

Investigations

• All patients with advanced HIV disease should be screened for common OIs including TB, cryptococcal meningitis and other common OIs depending of their presenting signs and symptoms

Major and Minor Presentations of IRIS

Major presentation	Minor presentation
Tuberculosis (TB) Mycobacterium avium complex (MAC) Cryptococcal meningitis Cytomegalovirus (CMV) retinitis Hepatitis B or C virus Progressive multifocal leukoencephalopathy (PML) Kaposi's sarcoma Cerebral toxoplasmosis Autoimmune diseases	Herpes simplex virus (HSV) and varicella zoster virus (VZV) Nonspecific dermatologic complications such as folliculitis and oral and genital warts

Management of IRIS

IRIS management is dependent on severity of symptoms and the following general guidance is recommended:

Severity of IRIS	Definition	Management

Mild	• Resolves over time in most patients
	• Symptomatic treatment is often sufficient
		• Treat the OI and manage the associated symptoms
		• Treat IRIS-associated inflammation:
		  ○ NSAIDS for discomfort associated with mild inflammation / fevers
		  ○ Inhaled steroids for bronchospasm or cough associated with mild pulmonary inflammation
		• Surgical intervention:
		  ○ Drainage of abscesses
		  ○ Excision of inflamed and painful lymph nodes

Severe	• Threatens a patient's functional state
	• Cause permanent disability
	• Potentially lead to death
	Examples:
	• Decline in pulmonary capacity from TB or MAC infection
	• Neurologic complications from cryptococcal infection
	• Loss of vision from CMV retinitis infection
		• Treat the OI and manage the associated symptoms
		• Manage the IRIS-associated inflammation:
		  ○ If NOT cryptococcal meningitis or KS: give 1 to 2 mg/kg prednisone for 1 to 2 weeks. Follow with a period of individualized tapering of the dose
		  ○ Do not use corticosteroids for the management of CM or KS- related IRIS
		• Closely monitor patients on corticosteroid therapy for:
		  ○ Hyperglycemia
		  ○ Hypertension
		  ○ Mental status changes
		  ○ Avascular necrosis
		  ○ Worsening of an existing infection
		  ○ Predisposition to a new infection (e.g. TB and CMV)

Annex 11: 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

Annex 12: TB Infection Control Assessment Tool

TB INFECTION CONTROL ASSESSMENT TOOL

Facility name:_____

Type of facility: _____

Level of care: _____

Name and title of person administering the interview: _____
_____

Name and title of respondent: _____
_____

Date assessment done (dd/mm/yyyy): _____/_____/_____

Instructions for completion:

- Circle the response most applicable to your institution. Total the scores in the place provided
- Retrieve last year's assessment and note improvements and declines in this year's assessment compared to last year's assessment

1. Supporting structures and activities to ensure implementation of TB infection control interventions.

	0	1	2
1.1. Has the facility TB IC risk assessment been conducted in the last 1 year	No		Yes
1.2. Is there a TB Infection Control Plan for the facility?	No		Yes
1.3. Does your facility have an Infection Prevention and Control Committee?	No		Yes
1.4. Did this committee meet within the last 4 weeks?	No		Yes
1.5. Is the TB infection control plan displayed in a public place?	No		Yes
1.6. Were TB infection control measures assessed within the last 1 month?	No		Yes
1.7. Was a CME on TB IC conducted in the last quarter?	No	Some staff	Yes
1.8. Were all HIV+ clients screened for TB symptoms (cough, loss of weight, night sweat) in the last 1 year?	No	Some (Proof available)	Yes (Proof available)
1.9. Were health talks given to waiting clients which included a message about TB symptoms and diagnosis?	No		Yes
1.10. Were any maintenance activities undertaken during the last 1 year on structures which improve TB infection control (e.g. air conditioning, fans, UVGI fittings)?	No		Yes
Total score (Maximum = 20)			

2. Administrative controls: Strategies to reduce generation of infectious aerosols:

	0	1	2
2.1. Are patients screened for cough at OPD?	No	Occasionally	Yes
2.2. Are patients educated in cough hygiene at OPD?	No	Occasionally	Yes
2.3. If patients cough, are they provided with masks/tissues to reduce infectious aerosols?	No	Occasionally	Yes
2.4. Are TB suspects/patients separated from those who are not?	No	Occasionally	Yes
2.5. Are TB suspects given priority to ensure shorter waiting times in outpatient facilities?	No	Occasionally	Yes
2.6. How many staff were trained on TB IPC in the last 1 year?	None	1	2 or more
2.6. Are there separate and ventilated facilities for sputum collection from suspects?	No	Yes, but not ventilated	Yes
2.7. What is the laboratory turn-around time for sputum AFB/ microscopy for the last sputum AFB result received?	> 48 hours	24 – 48 hours	< 24 hours
2.8. Did the facility screen all the HCWs for TB in the last 1 year?	None	Some	All
2.9. Did the facility offer confidential HIV counseling and testing to all HCWs in the last 1 year?	None	Some	All
2.10. Are posters displaying cough hygiene prominently displayed?	No		Yes
Total score (Maximum = 20)			

3. Environmental controls: Strategies to remove infectious aerosols after generation:

	0	1	2
3.1. Are the windows in your facility able to open?	No	Some	Yes
3.2. Are the windows in your facility kept open during working hours?	No	Occasionally	Yes
3.3. Are fans used to increase circulation of air in your area of work?	No	Occasionally	Yes
3.4. Do you know the direction of airflow in each consultation room in your facility?	For none	Only for some	Yes
3.5. Do staff in consultation rooms sit with their back towards the direction of airflow?	Uncertain	Occasionally	Yes
3.6. Are ultraviolet germicidal irradiation facilities in use in high risk areas?	No		Yes
3.7. In in-patient wards, are windows kept open at night?	No	Occasionally	Yes
Total score (Maximum = 14)			

4. Personal risk reduction strategies to reduce inhalation of infectious aerosols:

	0	1	2
4.1. How many staff were trained on TB disease in the last 1 year?	None	1	2 or more
4.2. Are N95 respirator/masks available this month?	No	Sometimes	Yes
4.3. Were N95 respirator/masks used by staff in high risk services within the last 1 month (e.g. TB, coughing queue)?	No	Sometimes	Yes
4.4. Are surgical masks available for coughing patients who cannot be separated?	No	Sometimes	Yes
Total score (Maximum = 8)			

NB:

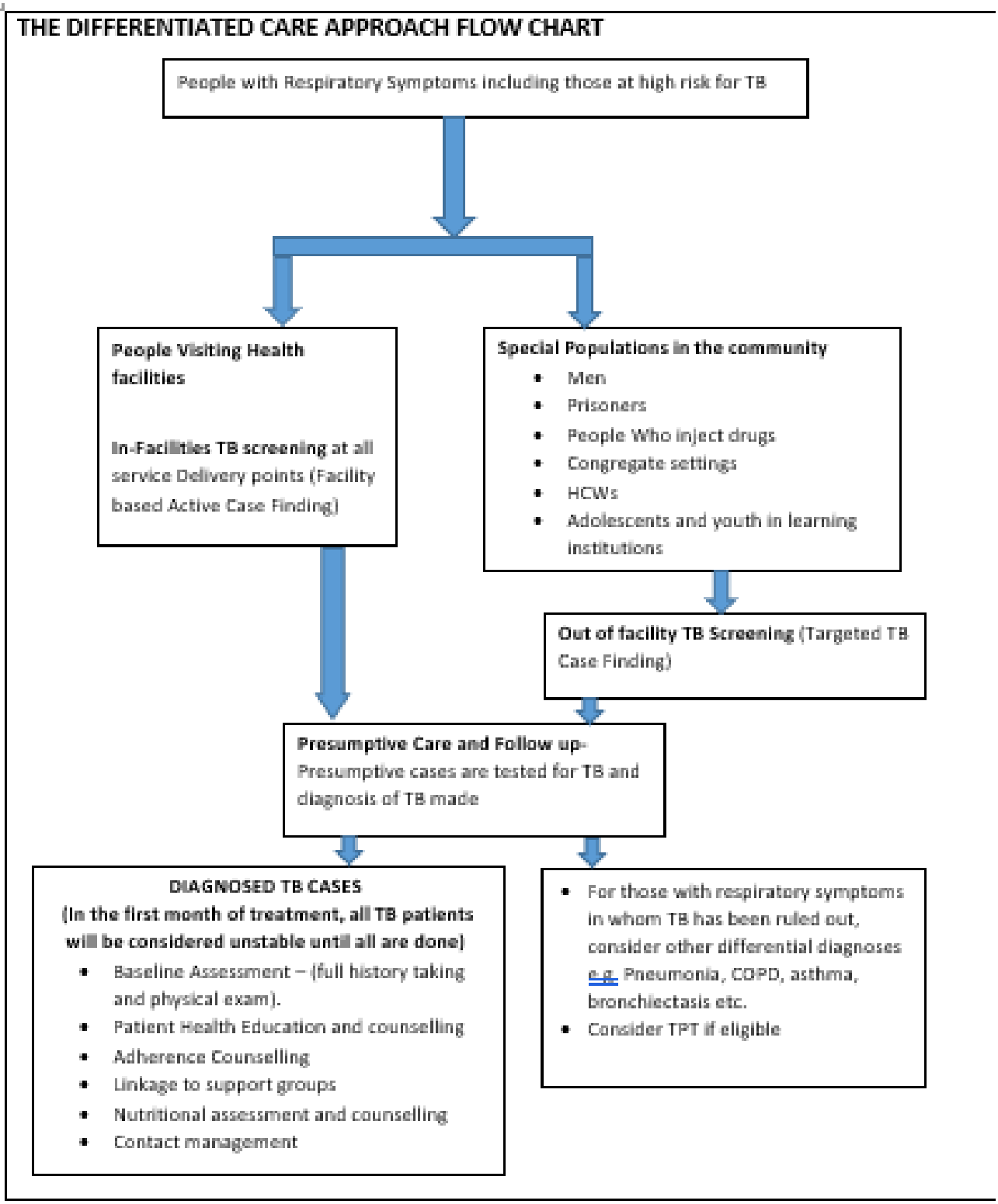
Note how many staff members were diagnosed with TB in the last year

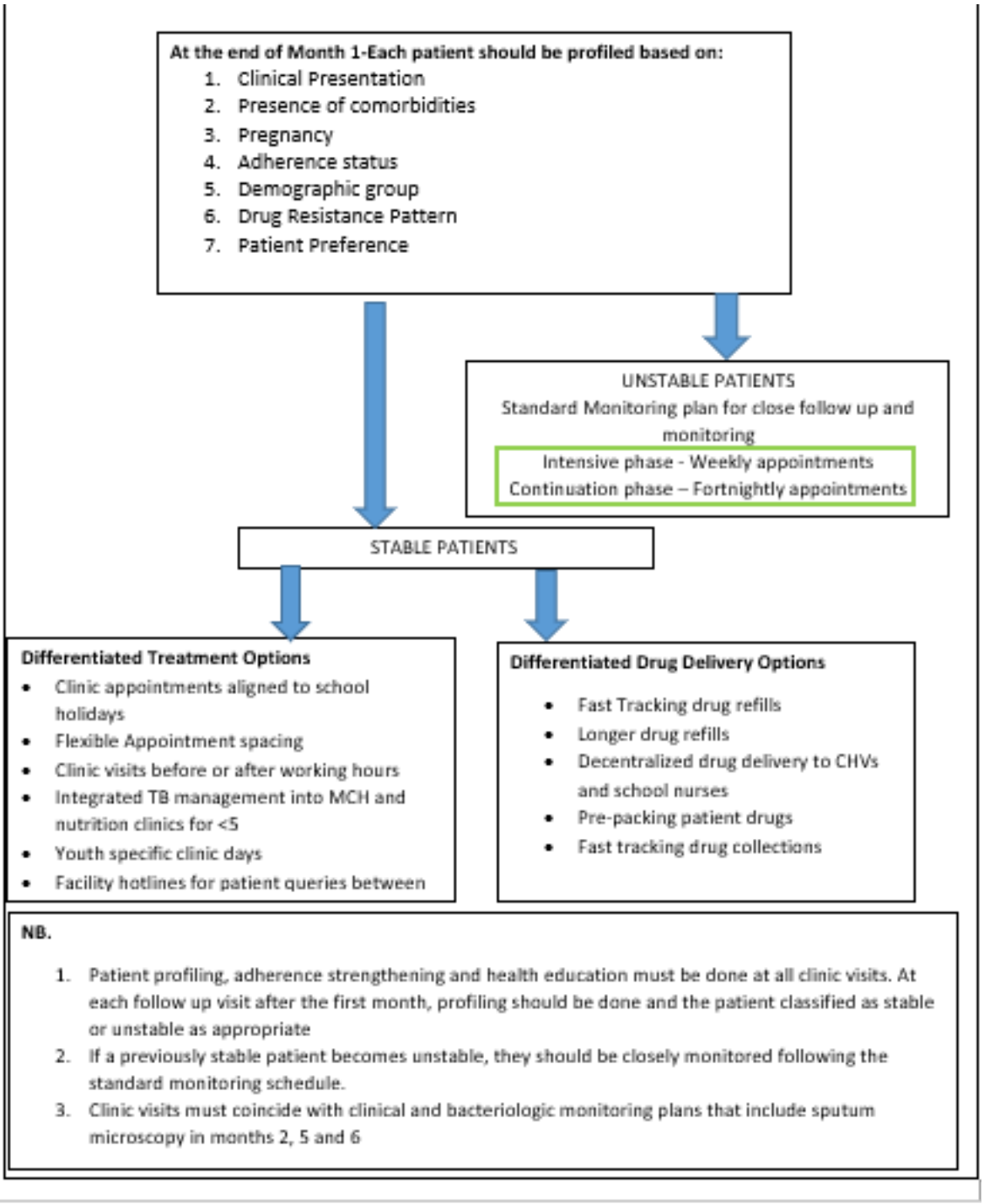
_____ _____

Describe the path of the patient, identify bottlenecks such as crowded interior waiting rooms, evaluate time separation and space separation, etc.

ANNEX 13: Approach to Differentiated Care for TB

THE DIFFERENTIATED CARE APPROACH FLOW CHART




At the end of Month 1-Each patient should be profiled based on:
1. Clinical Presentation
2. Presence of comorbidities
3. Pregnancy
4. Adherence status
5. Demographic group
6. Drug Resistance Pattern
7. Patient Preference
UNSTABLE PATIENTS
Standard Monitoring plan for close follow up and monitoring
Intensive phase - Weekly appointments
Continuation phase – Fortnightly appointments
STABLE PATIENTS
Differentiated Treatment Options
• Clinic appointments aligned to school holidays
• Flexible Appointment spacing
• Clinic visits before or after working hours
• Integrated TB management into MCH and nutrition clinics for <5
• Youth specific clinic days
• Facility hotlines for patient queries between
Differentiated Drug Delivery Options
• Fast Tracking drug refills
• Longer drug refills
• Decentralized drug delivery to CHVs and school nurses
• Pre-packing patient drugs
• Fast tracking drug collections
NB.
1. Patient profiling, adherence strengthening and health education must be done at all clinic visits. At each follow up visit after the first month, profiling should be done and the patient classified as stable or unstable as appropriate
2. If a previously stable patient becomes unstable, they should be closely monitored following the standard monitoring schedule.
3. Clinic visits must coincide with clinical and bacteriologic monitoring plans that include sputum microscopy in months 2, 5 and 6

ANNEX 14: Adherence Counselling Checklist for TB

PATIENT PROFILING TOOL		
• **Patient profiling, adherence strengthening and health education must be done at all clinic visits.** • **Presence of one indicator within the unstable category qualifies a patient as unstable.** • **At each follow up visit after the first month, profiling should be done and the patient classified as stable or unstable as appropriate.** • **If a previously stable patient becomes unstable, they should be closely monitored following the standard monitoring schedule.** • **Clinic visits must coincide with clinical and bacteriologic monitoring plans that include sputum microscopy in months 2, 5 and 6**		
Parameter	**Stable Patient**	**Unstable Patient**
Clinical Presentation	Clinically stable patient Improving clinical symptoms during treatment BMI >18.5 in adult/older children Smear negative at month 2	Unstable patient in respiratory distress. New/worsening respiratory symptoms during treatment BMI<18.5 Positive smear at month 2
Presence of comorbid conditions	No comorbidities present or when present, co-morbid conditions under control	Presence of uncontrolled comorbid conditions such as HIV, DM, NCDs, mental illness
Pregnancy status	Not pregnant	Pregnant
Adherence status and treatment outcome evaluation	No risk for poor adherence or poor treatment outcomes 100% compliance to clinic appointments and adherence counselling sessions	Risk for poor adherence Identified risk for poor treatment outcomes Missed appointments or adherence counselling sessions
Drug Resistance pattern	Susceptibility to all anti-TB medicines	Resistance to any anti-TB medicines
Age	Age>10years	Age <10yrs

Annex 15: Yellow Forms (ADR Reporting forms)

PV 1

MINISTRY OF HEALTH
THE PHARMACY AND POISONS BOARD
P. O. Box 27663-00506 NAIROBI
Tel: (020) 2716905 / 6 Ext 114 Fax: (020) 2713431/2713409.
Email: pv@pharmacyboardkenya.org

IN CONFIDENCE

☐ Initial Report
☐ Follow-up Report

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

NAME OF INSTITUTION: ..... INSTITUTION CODE: .....

ADDRESS: ..... CONTACT: .....

****

PATIENT'S NAME/ INITIALS: ..... IP OP. NO.: ..... D.O.B: .....

PATIENT'S ADDRESS: ..... WARD/CLINIC: ..... GENDER: ☐ Male ☐ Female
(Mark Number)

ANY KNOWN ALLERGY: ☐ No PREGNANCY STATUS: ☐ Not Pregnant WEIGHT (kgs): .....
☐ Yes (specify) ..... ☐ 1st Trimester
☐ 2nd Trimester HEIGHT (cm): .....
☐ 3rd Trimester

DIAGNOSIS: (what was the patient treated for) .....

.....

BRIEF DESCRIPTION OF REACTION: .....

.....

.....

LIST OF *ALL* DRUGS USED IN THE LAST 3 MONTHS PRIOR TO REACTION (include OTC and herbals) (use rear side of this form for additional drugs)	DOSE	ROUTE AND FREQUENCY	DATE STARTED	DATE STOPPED	INDICATION	TICK (√) SUSPECTED DRUG(S)
1						
2						
3						
4						
5						

SEVERITY OF THE REACTION: (Tick (√) only one)
☐ Mild
☐ Moderate
☐ Severe
☐ Fatal
☐ Unknown

ACTION TAKEN:
☐ Drug withdrawn
☐ Dose increased
☐ Dose reduced
☐ Dose not changed
☐ Unknown

OUTCOME:
☐ Recovering / resolving
☐ Recovered / resolved
☐ Requires or prolongs hospitalization
☐ Causes a congenital anomaly
☐ Requires intervention to prevent permanent damage
☐ Unknown

CAUSALITY OF REACTION: (Tick (√) only one)
☐ Certain
☐ Probable / Likely
☐ Possible
☐ Unlikely
☐ Conditional / Unclassified
☐ Unassessable / Unclassifiable

ANY OTHER COMMENTS: .....

.....

NAME OF PERSON REPORTING: ..... DATE: .....

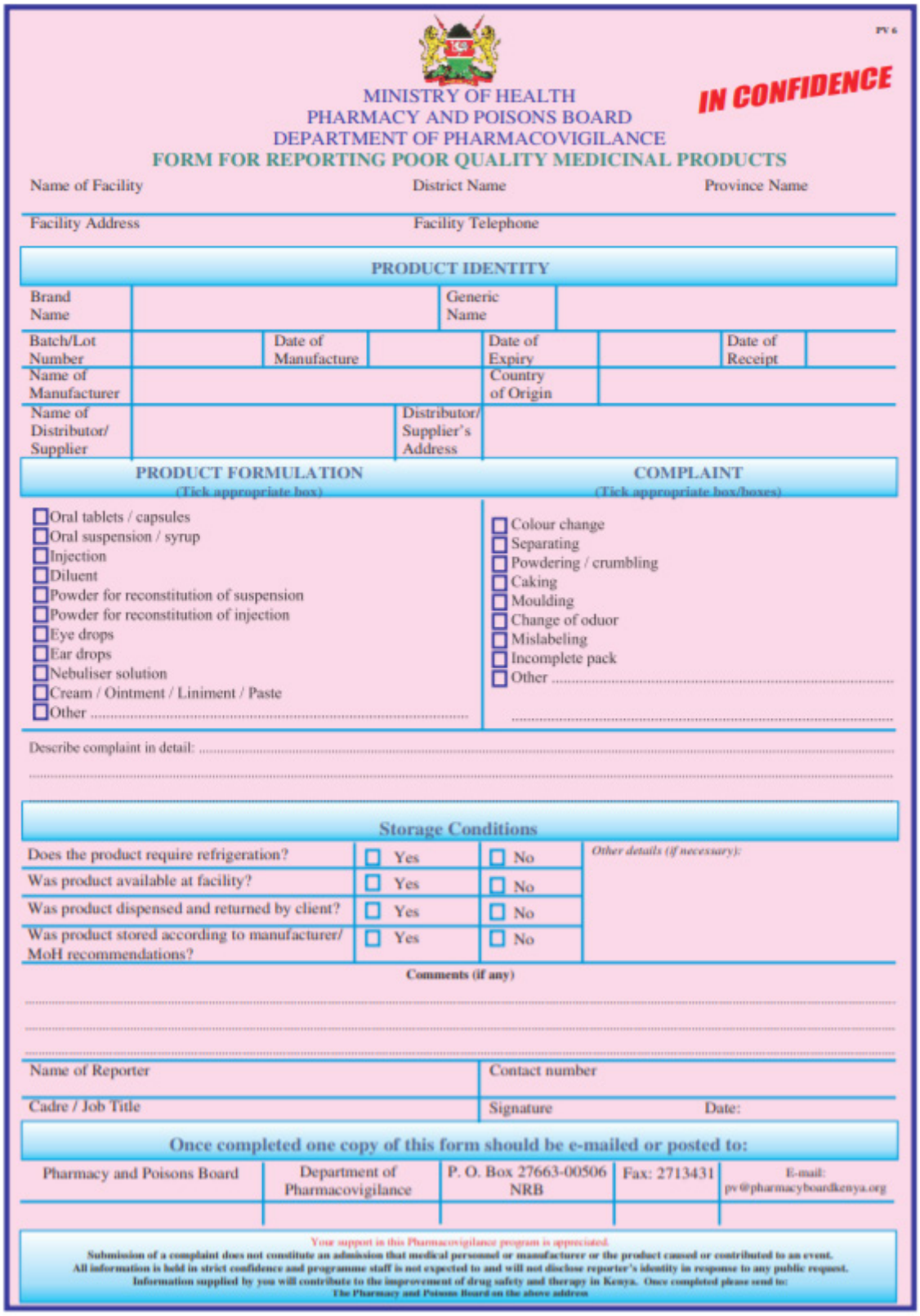
E-MAIL ADDRESS: ..... PHONE NO. .....

DESIGNATION: ..... SIGNATURE: .....

You need not be certain ... just be suspicious !

Your support in this Pharmacovigilance program is appreciated.
Submission of a complaint does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event.
Patient's identity is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.
Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya. Once completed please send to:
The Pharmacy and Poisons Board on the above address

Annex 16: Pink Form (Poor Quality medicine reporting form)



PV 6

IN CONFIDENCE

MINISTRY OF HEALTH
PHARMACY AND POISONS BOARD
DEPARTMENT OF PHARMACOVIGILANCE
FORM FOR REPORTING POOR QUALITY MEDICINAL PRODUCTS

Name of Facility | District Name | Province Name

Facility Address | Facility Telephone

PRODUCT IDENTITY

Brand Name			Generic Name				
Batch/Lot Number		Date of Manufacture		Date of Expiry		Date of Receipt	
Name of Manufacturer				Country of Origin			
Name of Distributor/ Supplier			Distributor/ Supplier's Address				

PRODUCT FORMULATION (Tick appropriate box)

- ☐ Oral tablets / capsules
- ☐ Oral suspension / syrup
- ☐ Injection
- ☐ Diluent
- ☐ Powder for reconstitution of suspension
- ☐ Powder for reconstitution of injection
- ☐ Eye drops
- ☐ Ear drops
- ☐ Nebuliser solution
- ☐ Cream / Ointment / Liniment / Paste
- ☐ Other .....

COMPLAINT (Tick appropriate box/boxes)

- ☐ Colour change
- ☐ Separating
- ☐ Powdering / crumbling
- ☐ Caking
- ☐ Moulding
- ☐ Change of oduor
- ☐ Mislabeling
- ☐ Incomplete pack
- ☐ Other .....

Describe complaint in detail: .....

Storage Conditions

Does the product require refrigeration?	☐ Yes	☐ No	*Other details (if necessary):*
Was product available at facility?	☐ Yes	☐ No	
Was product dispensed and returned by client?	☐ Yes	☐ No	
Was product stored according to manufacturer/ MoH recommendations?	☐ Yes	☐ No	

Comments (if any)

Name of Reporter | Contact number

Cadre / Job Title | Signature | Date:

Once completed one copy of this form should be e-mailed or posted to:

Pharmacy and Poisons Board	Department of Pharmacovigilance	P. O. Box 27663-00506 NRB	Fax: 2713431	E-mail: pv@pharmacyboardkenya.org

Your support in this Pharmacovigilance program is appreciated.
Submission of a complaint does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to an event.
All information is held in strict confidence and programme staff is not expected to and will not disclose reporter's identity in response to any public request.
Information supplied by you will contribute to the improvement of drug safety and therapy in Kenya. Once completed please send to:
The Pharmacy and Poisons Board on the above address

Annex 17: White Form (Patient Alert card)

MINISTRY OF HEALTH
PHARMACY AND POISONS BOARD
LENANA ROAD, NAIROBI P.O. BOX 27663 - 00506
TEL: (020) 2716905/6 Ext 114 Fax: (020)-2713431 / 2713409

PV 4

ADVERSE DRUG REACTION ALERT CARD

PATIENT NAME: .....

AGE: ..... **GENDER:** .....

DATE ISSUED: ..... **ADDRESS:** .....

SUSPECTED DRUG(S): .....

DESCRIPTION OF REACTION: .....

Other comments (if any): .....

.....

Tafadhali hakikisha umebeba kadi hii kila wakati. Kumbuka kumwonyesha mhudumu wa afya kadi hii unapo pata matibabu

Please carry this card with you at all times and remember to produce it to your health care professional at each time of consultation.

Annex 18: Criteria for Issue of Patient Alert Card

The alert card is given to:

- Patients who are hypersensitive / allergic / intolerant to a particular drug
- Patients who developed a 'near-fatal' reaction to any particular drug
- Patients who had a drug-induced morbidity to any drug
- Patients who had hospital admission due to an ADR to any drug
- Patients who developed an ADR which caused increase in the health care expenditure

Annex 19: WHO DRTB Medicine grouping

WHO 2018 grouping of medicines for Longer DR TB regimens			
Drug	**Activity against TB, Mechanism of action, and metabolism**	**Common Adverse reactions**	**Contraindications and special consideration**
GROUP A			
Levofloxacin (Lfx)	**Bactericidal:** has strong anti-TB activity. Cross-resistance with other fluoroquinolones but may not be complete. Data suggests greater activity than ciprofloxacin or Ofloxacin. Inhibits DNA gyrase	Nausea and bloating. Headache, dizziness, insomnia or tremulousness. Rare tendon rupture, arthralgias (can usually be treated symptomatically). Moderate QTcF prolongation, hypoglycaemia	Fluoroquinolones intolerance, prolonged QTcF, pregnancy (relative contraindication).
Moxifloxacin (Mfx)	**Bactericidal:** inhibits DNA gyrase; cross-resistance with other fluoroquinolones, but may be more active based on in vitro data	Nausea and diarrhoea. Headache and dizziness. Rare tendon rupture; arthralgias. Rare hepatotoxicity. QTc prolongation, hypo/ hyperglycemia	Fluoroquinolones intolerance, prolonged QTc
Bedaquiline (Bdq)	**Bactericidal:** Inhibits ATP synthesis. Mainly eliminated in faeces.	Nausea, vomiting, abdominal pain, loss of appetite, joint pain, headache. QT prolongation, hyperuricemia, phospholipidosis, elevated aminotransferases.	Do not use or discontinue Bedaquiline: Clinically significant ventricular arrhythmia. A QTcF interval of >500 ms Severe liver disease. Abnormal electrolytes. Use with caution in the following situations: Use with other QT prolonging drugs (see drug interactions) A history of torsade de pointes A history of congenital long QT syndrome A history of hypothyroidism and Brady arrhythmias

			A history of uncompensated heart failure Serum calcium, magnesium or potassium levels below the lower limits of normal
Linezolid (Lzd)	Has in vitro **bactericidal activity** – increasing clinical experience7; inhibits protein synthesis	Myelosuppression Diarrhoea and nausea. Optic and peripheral neuropathy Lactic acidosis – patients who develop recurrent nausea or vomiting.	Hypersensitivity to Oxazolidinones Symptoms of neuropathy (pain, numbness, tingling or weakness in the extremities
Group B			
Clofazimine (Cfz)	In vitro activity against *M. tuberculosis* without much in vivo data. Generally reserved for cases with few other options. Tissue half-life estimated to be around 70 days	Discoloration of skin, conjunctiva, cornea and body fluids. Dry skin, pruritus, rash, ichthyosis, and xerosis. Gastrointestinal intolerance. Photosensitivity.	Allergy to Clofazimine
Cycloserine (Cs)	**Bacteriostatic:** inhibits cell wall synthesis	**CNS toxicity:** including seizure, depression, psychosis and suicidal ideation Other side-effects include peripheral neuropathy and skin changes.	Relative contraindications include seizure disorder, psychotic disease or alcohol abuse
Group C			
Imipenem-cilastatin	Given that imipenem is rapidly degraded by renal proximal tubule dipeptidases, it is used in combination with the dipeptidase inhibitor, cilastatin. (Conversely, meropenem a similar drug as imipenem is stable to renal	**Common:** Diarrhoea, nausea, or vomiting. **Less common:** Seizure (noted with CNS infection), palpitations, pseudomembranous colitis.	Carbapenem intolerance; meningitis (use meropenem rather than imipenem).

	dipeptidases and requires no cilastatin). Cilastatin is partially metabolized renally.		
Meropenem	In vitro activity – very limited clinical experience (meropenem is stable to renal dipeptidases and requires no cilastatin).	Diarrhoea, nausea or vomiting. Seizure (noted with CNS infection), but rare compared to imipenem. Rarely elevated LFTs, haematologic toxicity, hypersensitivity	Carbapenem intolerance
***Delamanid (Dlm)**	Inhibition of the synthesis of the mycobacterial cell wall components, methoxy-mycolic and keto-mycolic acid. Delamanid disappears from plasma with a t1/2 of 30-38 hours. Delamanid is not excreted in urine.	Nausea, vomiting, and dizziness. QT prolongation	**Do not use or discontinue Delamanid** • Clinically significant ventricular arrhythmia. • A QTcF interval of > 500 ms (confirmed by repeat ECG). • Severe liver disease. • Serum Albumin less than 2.8. • Abnormal electrolytes. **Use with caution in the following situations (with more frequent ECG monitoring and evaluation of risk versus benefit):** • Use with other QT prolonging drugs (see drug interactions). • A history of torsade de pointes. • A history of congenital long QT syndrome. • A history of hypothyroidism and Brady arrhythmias. • A history of uncompensated heart failure. • Serum calcium, magnesium, or potassium levels below the lower limits of normal. **Use with caution in patients sensitive to lactose**

Ethambutol (Emb)	**Bacteriostatic:** inhibitor of cell wall synthesis; bactericidal only at the high end of the dosing range. At doses used over long periods of time, Ethambutol protects against further development of resistance	Retro bulbar neuritis (dose-related – exacerbated during renal failure).	Pre-existing optic neuritis; Visual changes on Ethambutol
Pyrazinamide (Pza)	**Bactericidal** for semi-dormant M. tuberculosis. Mechanism unclear	Gout (hyperuricemia) and arthralgias. Hepatotoxicity. Rash. Photosensitivity. Gastrointestinal upset	Allergy to pyrazinamide; severe gout
Amikacin (Am)	**Bactericidal:** Inhibits protein synthesis. Excreted primarily unchanged through the kidney.	Nephrotoxicity, ototoxicity	Relative contraindication in pregnancy and Hypersensitivity to aminoglycosides Caution with renal, hepatic, vestibular or auditory impairment.
Prothionamide (Pto)	**Weakly bactericidal:** blocks mycolic acid synthesis	Gastrointestinal upset and anorexia: Metallic taste. Hepatotoxicity. Endocrine effects: Gynaecomastia, hair loss, acne, impotence, menstrual irregularity, and reversible hypothyroidism	Side effects may be exaggerated in patients also taking Cycloserine
Kanamycin (Km)	**Bactericidal:** has strong anti-TB activity. Cross-resistance with Amikacin and some data suggesting cross-resistance with Capreomycin; inhibits protein synthesis	Nephrotoxicity: Ototoxicity (hearing loss) and vestibular toxicity: Increases with advanced age and prolonged use	Pregnancy (congenital deafness seen with streptomycin and Kanamycin use in pregnancy); hypersensitivity to aminoglycosides; caution with renal, vestibular or auditory impairment; patients with intestinal obstructions.

Para-amino salicylic acid (PAS)	**Bacteriostatic.**	Gastrointestinal distress Rare hepatotoxicity and coagulopathy Reversible hypothyroidism	Pregnancy (relative).
Others			
Isoniazid (Inh)	**Bactericidal:** Especially for rapidly dividing cells. Affects mycolic acid (cell wall) synthesis. Inclusion of isoniazid in the regimen of patients with strain W MDR-TB was also associated with improved outcomes	**Hepatitis** (age-related). Peripheral neuropathy. Hypersensitivity reactions. Other reactions, including optic neuritis, arthralgias, CNS changes, drug-induced lupus, diarrhoea, and cramping with liquid product	**Patients with high-level isoniazid resistance** who have failed an isoniazid-containing regimen should not receive isoniazid. History of allergic reaction to isoniazid
Rifampicin (Rif)	**Bactericidal:** inhibits protein synthesis; cross-resistance with other Rifamycins	Orange staining of body fluids Rash and pruritus Gastrointestinal upsets, flu-like syndrome Hepatotoxicity. Haematological abnormalities (thrombocytopenia, haemolytic anaemia).	**Rifamycins allergy;** due to drug interactions, may be contraindicated with concurrent use of certain drugs
Rifapentine (Rpt)	**Bactericidal:** same mechanism of action as Rifampin, inhibits RNA polymerase. 100% cross-resistant with Rifampin.	Red–orange staining of body fluids Rash and pruritus Hypersensitivity reaction Hepatotoxicity Haematological abnormalities	History of hypersensitivity to any of the Rifamycins (i.e. rifampin or rifabutin)

REFERENCES

American Diabetes Association. Standards of Medical Care in Diabetes –2021. Diabetes Care Jan 2021, 44 (Supplement 1) S15-S33

Classification of Diabetes Mellitus. Geneva: World Health Organization; 2019

DNTLD-P Annual Report 2019

EndTB Consortium. endTB Clinical and Programmatic Guide for Patient Management with New TB Drugs. Version 4.0; January 2018.

Forum of International Respiratory Societies (2017). The Global Impact of Respiratory Disease – Second Edition. Sheffi eld, European Respiratory Society, 2017

Forum of International Respiratory Societies. The Global Impact of Respiratory Disease – Second Edition. Sheffield, European Respiratory Society, 2017

Global Asthma Network (2018). The Global Asthma Report 2018. Global Asthma Network, 2018, Auckland, New Zealand

Global Initiative for Asthma (2020). Global Strategy for Asthma Management and Prevention.

Global Initiative for Chronic Obstructive Lung Disease (2020). Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease – 2020. Global Initiative for Chronic Obstructive Lung Disease, Inc.

https://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/pharmacovigilance/en/

https://pv.pharmacyboardkenya.org/: Guidelines for National Pharmacovigilance System in Kenya

https://my.clevelandclinic.org/health/diseases/17183-long-q-t-syndrome-lqts

https://www.mtaa.org.au/hearing-background

Human Rights Council - Progress report on the implementation of the principles and guidelines for the elimination of discrimination against persons affected by leprosy and their family members, 2016

Kenya Tuberculosis Patients Cost Survey, 2017

Lin Y, Harries A.D, Kumar A.M, Critchley J.A, van Crevel R, Owiti P, et al. Management of diabetes mellitus – tuberculosis: a guide to the essential practice. Paris, France: International Union against Tuberculosis and Lung Disease, 2019.

Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A (2013). ISAAC Phase Three Study Group. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: a global synthesis. Allergol Immunopathol (Madr). doi: 10.1016/j.aller.2012.03.001

Meghji J, Lesosky M, Joekes E*, et al (2020).* Patient outcomes associated with post-tuberculosis lung damage in Malawi: a prospective cohort study. *Thorax*; **75:**269-278. https://thorax.bmj.com/content/75/3/269

Ministry of Health, National Diabetes Prevention and Control Program. Kenya National Clinical Guidelines for the Management Of Diabetes Mellitus 2nd Edition, 2018.

Ministry of Health, National AIDS & STI Control Program. Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection in Kenya 2018 Edition. Nairobi, Kenya: NASCOP, August 2018.

Mungai BN, Joekes E, Masini E, et al (2021). It's not TB but what could it be? Abnormalities on chest X-rays taken during the Kenya National Tuberculosis Prevalence Survey. Preprint in Thorax. *https://www.medrxiv.org/content/10.1101/2020.08.19.20177907v1*

National Strategic Plan for TB, Leprosy and Lung Disease (2019-2023)

NTLDP - Kenya (2019). The National Tuberculosis, Leprosy and Lung Diseases Program: Annual Report 2019. 1–53. Ministry of Health, Kenya.

TB HIV Clinical Manual. Geneva: World Health Organization; 2004

Riza, Anca Lelia et al. "Clinical management of concurrent diabetes and tuberculosis and the implications for patient services." The Lancet. Diabetes & Endocrinology vol. 2,9 (2014): 740-53. doi:10.1016/S2213-8587(14)70110-X

Vikrant, S. (2019), Tuberculosis in dialysis: Clinical spectrum and outcome from an endemic region. Hemodialysis International, 23: 88-92

The Constitution of Kenya

The Patient's Charter for Tuberculosis Care: Patients' Rights and Responsibilities

Tuberculosis Gender Assessment in Kenya, 2018

WHO Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries. WHO/HTM/TB/2012.

World Health Organization (2019). Global Tuberculosis Report 2019. WHO/CDS/TB/2019.15. World Health Organization, Geneva, Switzerland

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