



MINISTRY OF HEALTH

## UGANDA NATIONAL TUBERCULOSIS AND LEPROSY CONTROL PROGRAMME

# **MANUAL FOR MANAGEMENT AND CONTROL OF TUBERCULOSIS AND LEPROSY**

*4TH EDITION  
2024*

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## LIST OF ABBREVIATIONS

6MWT	6 Minute Walking Test	MDR TB	Multi drug resistance Tuberculosis
AFB	Acid Fast Bacilli	MDT	Mult drug therapy
ANC	Antenatal care	MoH	Ministry of Health
ART	Antiretroviral therapy	MTB	Mycobacterium tuberculosis
BCG	Bacillus Calmette-Guerin	MTBC	Mycobacterium tuberculosis complex
BMI	Body Mass Index	MUAC	Mid Upper Arm Circumference
CAD	Computer aided diagnostic	mWRD	Molecular WHO recommended rapid diagnostics
CBC	Complete blood count	NAAT	Nucleic Acid Amplification test
CBR	Community-based rehabilitation	NGO	Non-governmental organisation
CHEW	Community health extension worker	NRH	National Referral hospital
CLF	Community Linkage Facilitator	NSP	National Strategic Plan
CNS	Central Nervous System	NTLP	National Tuberculosis and Leprosy Program
COPD	Chronic Obstructive Pulmonary disease	NTRL	National Tuberculosis Reference Laboratory
CPET	Cardiopulmonary Exercise Testing	NHLDs	National Health Laboratories and Diagnostic Services
CPHL	Central Public Health Laboratory	NMRL	National Microbiology Reference Laboratory
CPT	Cotrimoxazole preventive therapy	PB	Paucibacillary
CRP	C-reactive protein	PBC	Pulmonary bacteriologically confirmed
CXR	Chest Xray	PFT	Pulmonary Function Testing
DAT	Digital adherence technologies	PHP	Private health providers
DHO	District Health Officer	PITC	Provider- initiated testing and counselling
DLCO	Diffusing capacity of the lungs for carbon monoxide	PLHIV	People living with HIV
DM	Diabetes mellitus	PNFPs	Private not for profit
DOT	Directly observed treatment	POD	Prevention of disability
DSD	Differentiated Services Delivery	PR	Pulmonary rehabilitation
DST	Drug Susceptibility testing	PTB	Pulmonary Tuberculosis
DTF	Dolutegravir	PTLD	Post TB lung disease
DTLS	District TB and Leprosy Supervisor	PWD	Persons with Disabilities
DTU	Diagnostic and Treatment Unit	QoL	Quality of Life
EFV	Efavirenz	RIF	Rifampicin
ENL	Erythema Nodosum Leprosum	RPMT	Regional performance monitoring team
EPTB	Extra Pulmonary Tuberculosis	RR	Rifampicin Resistant
EEA	External quality assurance	RRH	Regional Referral Hospital
ESR	Erythrocyte Sedimentation Rate	RTLP	Regional TB and leprosy focal person
FDC	Fixed dose combination	SAM	Severe Acute Malnutrition
FEV	Forced Expiratory Volume	SAT	Self-administered treatment
FVC	Forced Vital Capacity	SRL	Supra national laboratory
GDP	Gross domestic product	TB	Tuberculosis
HCW	Health care worker	TBI	Tuberculosis Infection
HIV	Human Immunodeficiency Virus	TBM	Tuberculous Meningitis
HSD	Health subdistrict	TBST	Tuberculosis antigen-based skin test
IC	Infection Control	TCMPs	Traditional and complimentary medicine practitioners
ICF	Intensified case finding form	TPT	Tuberculosis Preventive Treatment
IGRA	Interferon-gamma release assay	TST	Tuberculin skin test
IPC	Infection, prevention control	UNHLS	Uganda National Health Laboratories
IRIS	Immune Reconstitution Inflammatory Syndrome	USD	United States dollars
KCCA	Kampala Capital City Authority	VDOT	Video Directly Observed therapy
LAMP	Loop-mediated isothermal amplification	VHT	Village Health Team
LED	Light Emitting Diodes	VHTs	Village health teams
LF-	Lateral flow urine lipoarabinomannan assay	VMT	Voluntary muscle testing
LAM		VST	Video-supported treatment
LFT	Liver function tests	W4SS	WHO four-symptom screen
LPA	Line Probe Assay	WHO	World Health Organization
LTBI	Latent tuberculosis infection	XDR TB	Extremely resistant Tuberculosis
M.tb	Mycobacterium Tuberculosis		
MB	Multibacillary		

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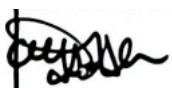
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## PREFACE

The ministry of health national TB and leprosy program (NTLP) last updated the guidelines on the management and control of TB and leprosy (NTLP manual) in 2017.

The WHO in 2021, released the consolidated guidelines on tuberculosis control and operational guides to help countries adapt and incorporate the new guidelines in their national guidelines. The WHO guidelines highlight new recommendations for tuberculosis and leprosy control, including systematic screening of TB among risk groups using sensitive tools like digital X-ray and CAD, strengthening TB preventive treatment at health system across the cascade of care for TB, enhance provider and community awareness on importance of TPT, and ensure rapid access to latest tools for detection of TB infection as well as shorter TPT regimens.

Additionally, the WHO guidelines recommend simple and easier tests like Simple -one-step stool analysis for TB diagnosis in children, shorter regimen for treatment of TB in children and all-oral regimen for management of drug resistant TB.

In order to adapt these new WHO recommendations at country level, the National Tuberculosis and leprosy program (NTLP) initiated the process to revise and update the 3rd edition (2017) of the NTLP manual, a document that provides overarching policy guidance on TB and leprosy control in Uganda.

The key technical persons from the MOH-NTLP were consulted and contributed in the review and development of the initial draft of the NTLP manual and this was followed by a technical consultative meeting to obtain input from experts with the stakeholders including technical officers from other departments in the ministry of health, clinicians, academia and researchers to obtain consensus.

While leprosy control has been sustained, there are challenges in reducing the burden to even lower levels in the context of the scattered high burden sites or "hot spots" in an otherwise low endemic setting and the dwindling knowledge about leprosy in the community as well as the health service providers. Furthermore, the burden of disability due to leprosy remains high

This revised manual provides an update on the key areas for TB and leprosy control and pays special attention to the key role of the district TB/leprosy supervisors (DTLS).

It is envisioned that the updated guidelines will increase access to timely and quality TB diagnosis and treatment including within primary health care settings. The manual should be a ready reference for the various service providers but also serve to meet the needs of any other people with a stake in the care of tuberculosis and leprosy patients as well as the provision of preventive services.



Dr Stavia Turyahabwe

Commissioner, National Disease Prevention and Control

## **FOREWORD**

Tuberculosis is a leading cause of morbidity and mortality world-wide and Uganda is among the 30 high TB and TB/HIV burden countries globally. Uganda has made significant progress in achieving the global targets of 90% treatment coverage, 90% treatment success and reduction in TB mortality by over 50%. The country is however far from attaining the End TB target of reduction in the TB incidence to less than 60/100,000 by 2030.

The national tuberculosis and leprosy strategic plan (NSP) aimed at reducing the TB incidence by 20% from 200/100,000 population in 2020/21 to 160/100,000 in 2024/25, but there has been minimal impact on the TB incidence, estimated at 198/100,000 in 2024 despite implementation of various strategic interventions to improve TB case finding and treatment outcomes. This highlights the task ahead for Uganda to achieve the ambitious global target of ending tuberculosis by the year 2035.

Uganda has also made significant progress in leprosy control. The country already achieved the target of elimination of leprosy as a public health problem. However, several new cases of leprosy continue to be notified annually. Many of these have established disabilities and a significant proportion are children.

The ministry of health (MOH) national tuberculosis and leprosy control division (NTLD) is charged with the responsibility of providing strategic guidance in tuberculosis and leprosy control in the country through developing policy guidelines, capacity building and support supervision of subnational structures.

The MOH/NTLP last published the national guidelines for Tuberculosis and Leprosy control (NTLP manual 3rd edition) in 2017. The manual contains information on the structure and functions of the NTLP, diagnosis and management strategies for tuberculosis and leprosy.

In 2021, WHO released the consolidated guidelines on tuberculosis control and operational guides to help country level adaptations. These new recommendations include the need to scale up new tools for TB screening and diagnosis, tests for latent TB infection and shorter treatment regimen for paediatric TB and drug resistant TB as well as TB preventive treatment. The revision of the NTLP manual was therefore necessary to enable adaptation of the new WHO recommendations and align the national guidelines with global policies

The Ministry of Health is committed to provision of high quality and people centred care for people affected by TB and leprosy. I congratulate the NTLP and stakeholders on this achievement. I recommend this manual to all involved in TB and Leprosy prevention and care in Uganda and beyond.

For God and my Country.



Dr Charles Olaro

Ag. Director General of Health Services, Ministry of health

## **CHAPTER 1: INTRODUCTION**

### **1.1      Geography and Demography**

Uganda, is popularly known as the 'The Pearl of Africa' and is located along the equator and lies in the Eastern part of Africa. It is a land locked country and neighbours Kenya in the East, Tanzania in the South, Rwanda in the Southwest, Democratic Republic of Congo in the West and Sudan in the North. It covers a surface area of 241,555 sq.km. Uganda is home to 45% of Lake Victoria, which is Africa's largest lake by area and the world's largest tropical lake.

The country is divided into 4 traditional regions i.e., Eastern, Western, Northern and Central; each with administrative units. The administrative units are arranged in a hierarchical order and include: Districts (146), Counties (322), Municipalities (39), sub counties (1488), parishes (7553) and villages (58,197). The total number of districts is currently 146.

The annual population growth rate is 3.1% per annum, with the average number of persons per household standing at 4.7. Current population estimates put the population of Uganda at 42.8 million. At 51%, females are the majority of the population. The life expectancy stands at 63 years.

As of 2020, the GDP per capita stood at USD 883.9, and the annual core inflation has gradually increased to 4.7%.

### **National health service system**

Uganda's national health system constitutes of all institutions, structures and actors which all aim at achieving and sustaining good health. There are both public and private care providers. The public sector includes all government health facilities, while the private health delivery system consists of private health providers (PHPs). The private healthcare providers fall under 3 categories i.e., private for profit (PFPs), private not for profit (PNFPs) providers (including the faith-based organisations) and the traditional and complimentary medicine practitioners (TCMPs).

The health care system in Uganda is decentralised right from the ministry level up to the village, district and health sub district levels. Districts and health sub-districts (HSDs) play a key role in the delivery and management of health services at district and health subdistrict (HSD) levels respectively.

The Ministry of Health (MoH) provides leadership for the health sector and takes a central role and responsibility in the delivery of a wide range of health services including curative, preventive, promotive, palliative and rehabilitative services to the people of Uganda. The public health facilities are structured into National Referral hospitals (NRHs) and Regional Referral Hospitals (RRHs), general hospitals, health centre IV, HC III and HC II. The HC I has no physical structure but a team of people (the Village Health Team (VHT)) which works as a link between health facilities and the community.

## Burden of Tuberculosis and leprosy

### **Burden of Tuberculosis**

Uganda is one of the 30 high TB burden countries, in addition to being a high HIV/TB burden country. Despite efforts to increase TB case finding, a substantial number of patients are still missed. In 2020, up to 24% of TB cases were missed and 16.9% of the missed TB cases were children<sup>1</sup>. In 2020, up to 90,000 incident TB cases were reported. The incidence of TB stands at 196/100,000 while the national TB prevalence survey conducted in 2015 put the TB prevalence at 253/100,000 population.

In 2020, the treatment coverage was 68%. As of 2021, the TB treatment success rate for Drug sensitive TB stood at 83%, TB related mortality at 7.1% while the lost to follow up rate was 8.1%. During the same time, the TPT uptake in the under 5 was 33% and of the under- 5 initiated on TPT, up to 79% completed the treatment (NTLP Bulletin). In 2020, 556 rifampicin resistant TB patients were notified, and of these 121 (21.8%) were confirmed MDR TB patients. The treatment success rate for this cohort was 80% (cured=234, treatment completed=204), with the mortality in the cohort standing at 12%.

TB management in this sector still faces several challenges. Despite 58% of the people initiating their health care seeking from the private sector, data showed that only 20% of TB notifications come from the private sector. Efforts have been made to accredit and regulate more private health facilities to ensure involvement in TB screening and TB treatment, and this is to continue together with the engagement of other private sector players beyond health. The goal for this is to promote standardized TB care in the private sector which will in turn result in increased TB case detection, enrolment on appropriate TB treatment, improved cure rates and reduced risks of drug resistance development.

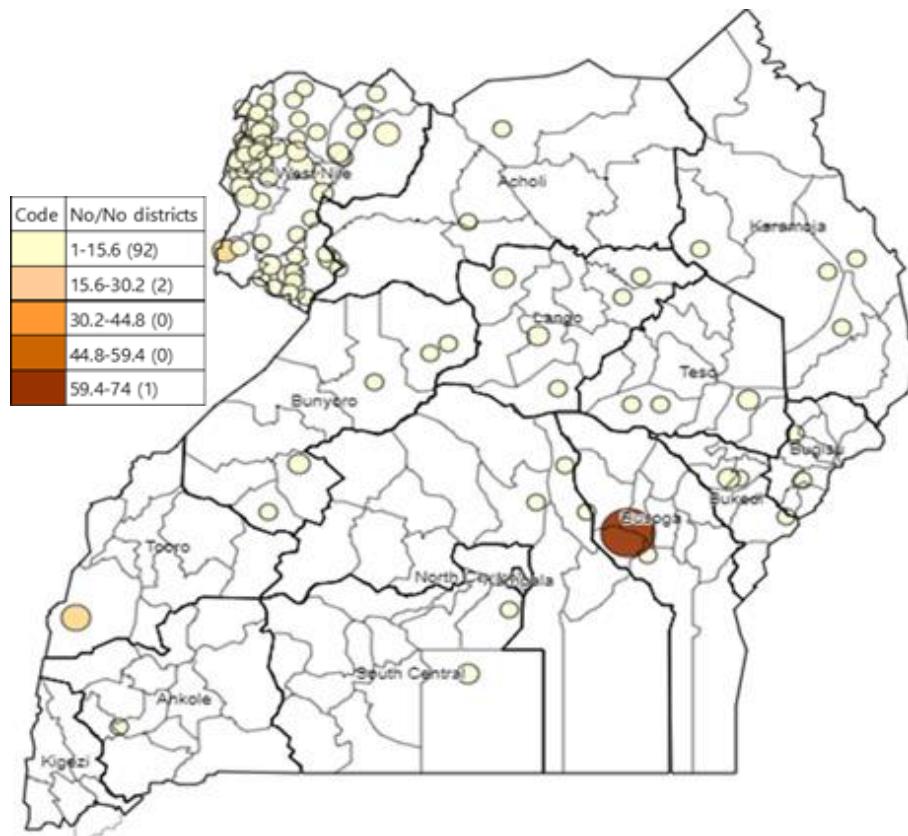
### **Burden of Leprosy**

The elimination of leprosy (defined as achieving a point prevalence of below 1 per 10,000 population) as a public health problem which was first attained in 1994 and has been sustained at national level. Since 2004, elimination has also been achieved at regional level. However, there has been a gradual increase of the number of cases registered in Uganda annually over the past five years from 165 cases in 2017 to 388 cases in 2021. The number of new cases among children and those identified with major physical disabilities is high at 13% and 21.5% respectively.

### **Distribution of new and relapse leprosy cases**

There are a number of leprosy cases being reported in all regions of the country and in some districts, there are pockets of high leprosy disease. These districts include: West Nile region (Yumbe, Koboko, Arua, Zombo districts), Lango region (Kwania, Lira, Amolatar and Apac districts) and Acholi Region (Pader, Kitgum, Gulu).

Figure 1 Map showing leprosy cases in Uganda (2021)



### The National Tuberculosis and Leprosy Program (NTLP)

The NTLP, is a disease control program under the department of National Disease Control of the Ministry of Health (MoH). The NTLP is charged with performing the national core function of TB and Leprosy control through:

1. Establishment of country wide facilities for quality diagnosis and treatment of TB and leprosy
2. Coordination and supervision of the implementation of TB and leprosy prevention and care
3. Prevention and management of leprosy-related disabilities

The NTLP follows internationally accepted strategies of TB control. The World Health Organization (WHO) designed a new strategy called the End TB strategy which was adopted by the 67th World Health Assembly on May 19, 2014. The recently developed NTLP strategic plan (NSP) for the period 2021-2025 is in line with Global and National commitments including the End TB strategy. The NSP represents a new approach to the elimination of TB and Leprosy through a patient centred approach. The End TB strategy provides a unified response to end TB deaths, disease, and suffering. The strategy has three pillars and 10 components, and is based on four principles.

#### **Pillar 1: Integrated, patient centred care and prevention**

##### Components

- Early diagnosis of TB including universal drug susceptibility testing, and systematic screening of contacts and high-risk groups
- Treatment of all people with TB including drug resistant TB, and patient support
- Collaborative TB/HIV activities and management of comorbidities
- Preventive treatment of persons at high risk; and vaccination against TB

## **Pillar 2: Bold policies and supportive systems**

### Components

- Political commitment with adequate resources for TB care and prevention
- Engagement of communities, civil society and all public and private care providers
- Universal health coverage policy and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
- Social protection, poverty alleviation and actions on other determinants of TB

## **Pillar 3: Intensified research and innovations**

### Components

- Discovery, development and rapid uptake of new tools, interventions and strategies
- Research to optimize implementation and impact and promote innovations

## **Organizational structure of the NTLP**

The NTLP is a central unit that coordinates TB and Leprosy activities in the country. It is headed by the Program Manager and is supported by a number of officers who coordinate the following units: Prevention and health promotion, monitoring and evaluation, care and treatment services, laboratory services, and policy and regional TB and leprosy services. Under the above units, there are focal officers for specific program functions.

At the regional level, management and supervision of TB and Leprosy services is performed by the regional TB and leprosy focal person (RTLP). There are currently 12 regions which are aligned to the 12 Ministry of health (MoH) Regional performance monitoring teams (RPMT) structure. At the district level, the District Health Officer (DHO) is responsible for the management of health service delivery including TB and Leprosy prevention and care. The DHO assigns a district health team member i.e., District TB and Leprosy Supervisor (DTLS) with the responsibility of overseeing TB and Leprosy care and prevention services in the district.

At the Health Sub-district level (HSD), the in-charge of the HSD is responsible for the management of health service delivery including TB and Leprosy care and prevention services. A health worker is assigned the responsibility of overseeing TB and Leprosy care and prevention services at the HSD level and this person is referred to as the Health Sub-district focal person. At the district, HSD and health facility level, TB and leprosy care and prevention services are integrated into the general health services. Table 1 below summarizes the responsibilities:

*Table 1 Responsibilities for different levels with regard to TB and Leprosy control*

<b>Level of management</b>	<b>Responsibilities</b>
<b>National level (Central Unit) (Programme manager) including NTRL</b>	Formulating and revising policies and guidelines Planning, including development of strategic and operational plans Resource mobilization Setting standards and quality assurance, advocacy, coordination and networking Training Monitoring and evaluation TB and Leprosy Surveillance Operational research
<b>Regional level (Regional TB and leprosy focal person)</b>	Assist the Program manager with the above responsibilities Supervision of district TB and Leprosy activities Mentoring of DTLS Advocacy, coordination and networking in the region Dissemination of policies and guidelines Training Monitoring and evaluation Operational research
<b>District level (District Health Officer)</b>	Plan and prioritize TB and Leprosy care and prevention interventions Ensure compliance to national policy and guidelines Support and supervise the DTLS, district laboratory focal person (DLFP) and Health sub-district in-charges Identify training needs and support training Monitor and evaluate TB and Leprosy care and prevention interventions Resource mobilization Advocacy, coordination and networking in district Operational research
<b>District TB and leprosy supervisor</b>	Ensure critical activities are included in district plans Supervise health workers implementing TB and Leprosy care and prevention services Ensure compliance to national policies and guidelines Train, support and supervise HSD focal persons and sub-county HWs Ensure availability of drugs at health facilities Validate data on TB and Leprosy Update district registers
<b>Health sub district in charge and/ focal person</b>	Support the DTLS to ensure that the above activities are done at HSD level Advocacy, coordination and networking in health sub-district
<b>Community level</b>	Comprise the Village Health Team and local council III Suspicion and referral of presumptive TB Treatment support to patients

### **The Leprosy control strategy**

A new global leprosy strategy for 2021-2030 has been set. The Global Leprosy Strategy 2021- 2030: Towards Zero Leprosy and focuses on interrupting transmission and achieving zero autochthonous cases.

The goal of the strategy is to eliminate leprosy, which is defined as interruption from transmission. It has 4 global targets, to be achieved by 2030. The global targets by 2030 are as follows:

- 120 countries with zero new autochthonous cases
- 70% reduction in annual number of new cases detected
- 90% reduction in rate per million population of new cases with grade-2 disability (G2D)
- 90% reduction in rate per million children of new child cases with leprosy

The Global Leprosy Strategy 2021-2030 is also based on four strategic pillars:

1. Implement integrated, country-owned zero leprosy roadmaps in all endemic countries
2. Scale up leprosy prevention alongside integrated active case detection
3. Manage leprosy and its complications and prevent new disability
4. Combat stigma and ensure human rights are respected

## Network of TB laboratory services in Uganda

TB laboratory services in Uganda are delivered through a network of laboratories:

1. Microscopy Sites: Diagnostic TB units (DTUs) performing microscopy have expanded from 303 in 2006 to over 1,700 by 2022.
2. Molecular Diagnostics (mWRD): These include Nucleic Acid Amplification Tests (NAAT), such as Xpert MTB/RIF Ultra, which is widely used in Uganda with 358 machines installed across 296 facilities as of 2024. Other deployed NAATs include Truenat, TB LAMP, and LPA. These genotypic methods offer speed, standardization, and scalability, particularly for managing drug-resistant TB.
3. Culture and Drug Susceptibility Testing (DST): WHO recommends one TB culture lab per 5 million people and one DST lab per 10 million. Uganda has three TB culture labs in the public and private sectors.

## National TB Reference Laboratory (NTRL):

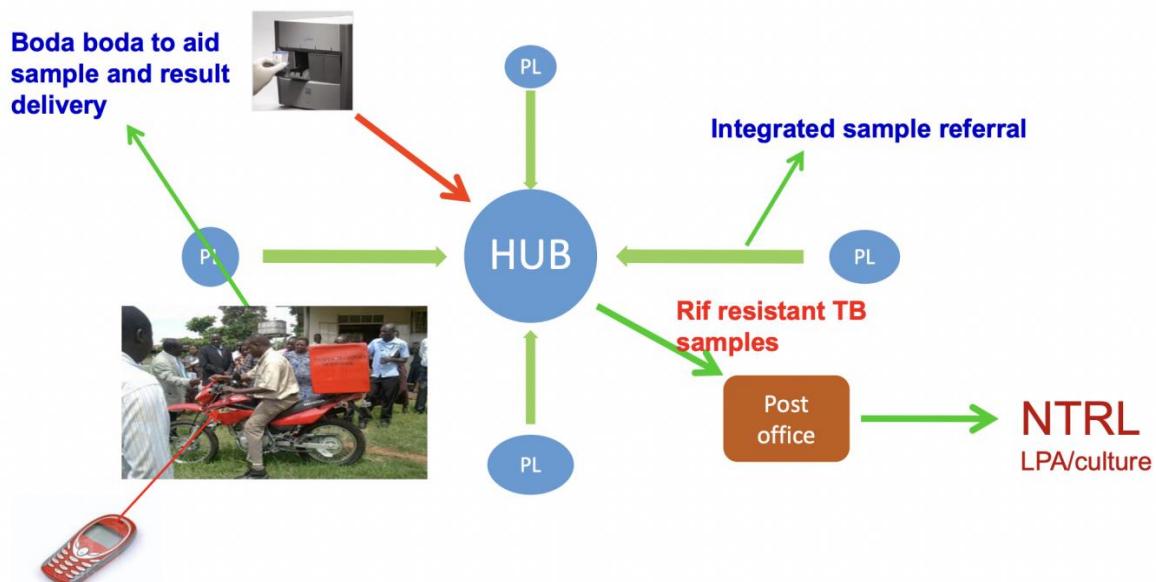
Established under the NTLP, NTRL leads the national TB diagnostic network, providing referral services, technical guidance, and support to reduce the TB and leprosy burden. Accredited under ISO 15189 in 2013 and elevated to a Supra-national TB Reference Laboratory (SRL), it supports over 18 countries in East and Central Africa and holds ISO 17043 and IACET accreditations. Currently, it does not provide similar services for leprosy.

## Network System for sample transport and transmission of results

Established in 2008 and integrated with the Hub system in 2015, Uganda's TB specimen referral system facilitates sample transport to Xpert MTB/RIF facilities and the NTRL.

The hub network, comprising 100 strategically located hubs, serves 20-30 health facilities within a 40-kilometer radius. Each hub, equipped with enhanced infrastructure, staff, and quality systems, analyses routine and referred samples. Motorcycle riders ensure efficient transport of samples and results, including rifampicin-resistant cases sent to NTRL for further testing. To enhance efficiency, the LabXpert system enables real-time transmission of results to referring health facilities.

Figure 2 The Hub system for TB specimen transport and referral



### External Quality Assessment (EQA)

To be reliable, laboratories performing microscopy, culture and molecular tests must participate in external quality assurance (EQA) programs. NTRL has the mandate to ensure Quality of TB diagnostics at all levels of the country's network through regular training and support supervision and initiation and maintenance of a National External assessment system for all TB testing laboratories. NTRL currently offers proficiency testing (PT) EQA materials for the GeneXpert, Truenat, LF-LAM, Microscopy (for ISO accredited/Preparing for accreditation laboratories) participating laboratories in two Rounds one in February and the other in August per year. NTRL also coordinates of a blinded Rechecking EQA scheme for all the non-accredited microscopy labs in the country.

**External Quality Assurance for sputum microscopy:** Sputum microscopy is kept reliable if laboratories participate in external quality assurance (EQA) such as blinded rechecking. In blinded rechecking, all examined TB slides are stored chronologically in a slide box and at the end of the quarter, a supervisor like the DTLS will randomly select at least 10 slides that will be re-examined at another laboratory (2nd control), usually a higher-level laboratory like the district hospital. The 2nd control laboratory will not be availed with the original results of the peripheral laboratory hence maintaining the blinding process of slide rechecking. Any discordance between the peripheral and 1st control laboratory is harmonized by a higher-level laboratory like the regional referral hospital or National Tuberculosis Reference Laboratory. The rechecking is done on a quarterly basis and EQA feedback reports should be returned to the peripheral laboratories so appropriate corrective actions can be implemented as and when need arises.

The process involves the examination of previously prepared slides to see if:

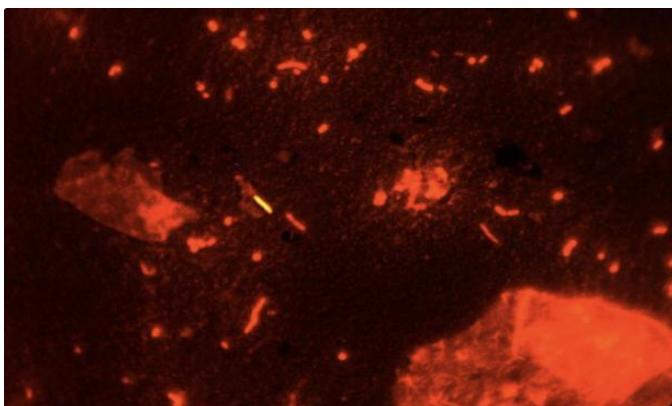
- Slides were prepared properly
- Slides were examined, and the reported results (positive or negative) are correct
- Recommended laboratory procedures are followed
- Safety measures are adhered to

## CHAPTER 2: TUBERCULOSIS

### TUBERCULOSIS IN HUMANS

TB is an airborne disease caused by the bacterium *Mycobacterium tuberculosis* (*M. tuberculosis*) (Figure 5). *M. tuberculosis* and seven very closely related mycobacterial species (*M. bovis*, *M. africanum*, *M. microti*, *M. caprae*, *M. pinnipedii*, *M. canetti* and *M. mungi*) together comprise what is known as the *M. tuberculosis* complex. Most, but not all, of these species have been found to cause disease in humans, however the most common cause is mycobacterium tuberculosis. *M. tuberculosis* organisms are also called acid fast bacilli because they retain a red dye after washing with alcohol following staining.

Figure 3 *M. tuberculosis* in a sputum smear is stained using fluorescent auramine with acridine orange counterstain (CDC)



### Transmission of TB

*Mycobacterium tuberculosis* spreads through airborne droplet nuclei (1–5 microns) expelled by individuals with pulmonary or laryngeal TB when coughing, sneezing, or speaking. These droplets can remain suspended for hours and are inhaled into the lungs, where they trigger immune responses that may result in latent TB infection (LTBI) or active TB disease. TB is not transmitted via surface contact.

Transmission is more likely under conditions such as:

- Poor ventilation in closed environments
- High bacterial load in sputum
- Close, prolonged contact with an untreated, bacteriologically confirmed TB patient
- High community TB prevalence

Conversely, occasional contact or extra-pulmonary TB reduces the risk of infection.

***M. tuberculosis* is carried in airborne particles, called droplet nuclei, of 1–5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout or sing**

### Infection and Development of TB Disease

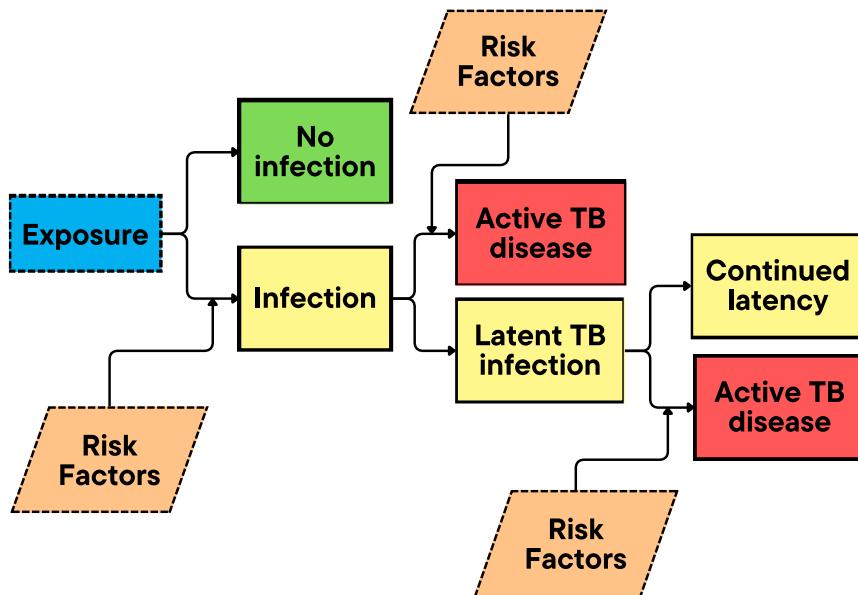
When infected for the first time, inhaled bacilli are ingested by alveolar macrophages. Most are destroyed, but some may survive and spread, triggering an immune response. In 90% of cases, the infection is contained, forming granulomas and leading to LTBI, where dormant bacilli persist. LTBI can be detected 2–8 weeks post-infection using tests like TST, TBST, or IGRA.

In 10% of individuals, weakened immunity allows bacilli to multiply, progressing to active TB disease, often in those with risk factors like HIV, diabetes, or malnutrition. Active TB can develop soon after infection or years later.

**Persons with LTBI have *M. tuberculosis* in their bodies, but do not have TB disease and cannot spread the infection to other people. A person with LTBI is not regarded as a case of TB.**

In most cases, TB disease results from reactivation of dormant bacilli, leading to tissue damage, commonly in the lungs. This post-primary disease is the predominant form of TB in adults. Active TB patients are infectious and require bacteriological testing for confirmation.

*Figure 4 Infection and Development of TB Disease*



Refer to Table 2 for differences between LTBI and TB disease

Clinically, TB is divided into two groups: Pulmonary TB and Extra pulmonary TB

- Pulmonary TB: is TB that involves the lungs. It is the most common form of TB and accounts for approximately 80 percent of all the patients with TB. These patients, particularly the bacteriologically confirmed ones can transmit the bacilli to others.
- Extra-pulmonary TB: is TB that occurs in organs of the body other than the lungs (including the pleura). These patients are unlikely to transmit the bacilli to other people.

NB: In the TB program setting, a TB patient who has both pulmonary and extra-pulmonary TB should be classified as a pulmonary TB patient since this category is of public health importance

*Table 2 Differences between Latent TB infection (LTBI) and TB disease*

LTBI vs. TB Disease	
Person with LTBI (Infected)	Person with TB Disease (Infectious)
Has a small amount of TB bacteria in his/her body that are alive, but inactive	Has a large amount of active TB bacteria in his/her body
<b>Cannot</b> spread TB bacteria to others	May spread TB bacteria to others
Does <b>not</b> feel sick, but may become sick if the bacteria become active in his/her body	May feel sick and may have symptoms such as a cough, fever, and/or weight loss
Usually has a TB skin test or TB blood test reaction indicating TB infection	Usually has a TB skin test or TB blood test reaction indicating TB infection
Radiograph is typically normal	Radiograph may be abnormal
Sputum smears and cultures are negative	Sputum smears and cultures may be positive
Should consider treatment for LTBI to prevent TB disease	Needs treatment for TB disease
Does <b>not</b> require respiratory isolation	May require respiratory isolation
<b>Not</b> a TB case	A TB case

## Zoonotic Tuberculosis

Zoonotic tuberculosis (TB) in humans is caused by *Mycobacterium bovis*, a member of the *M. tuberculosis* complex. It often affects extrapulmonary sites and can be clinically indistinguishable from TB caused by *M. tuberculosis*. *M. bovis* primarily affects cattle, the main animal reservoir, and is endemic in many parts of the world. The main transmission route to humans is indirect, primarily through the consumption of unpasteurized milk and dairy products. Less commonly, it is transmitted through raw or undercooked contaminated meat, or through direct airborne contact with infected animals or animal products.

## Challenges in Managing Zoonotic Tuberculosis

- Common diagnostic procedures do not differentiate *M. tuberculosis* from *M. bovis*, leading to underdiagnosis of zoonotic TB.
- *M. bovis* is naturally resistant to pyrazinamide, a first-line TB treatment, which complicates treatment, especially without drug susceptibility testing.
- Zoonotic TB is often extrapulmonary and may be misdiagnosed, delaying treatment initiation.
- Strategies to Reduce Transmission at the Animal-Human Interface
  - Safer food practices: Follow the WHO's Five Keys to Safer Food to reduce foodborne transmission:
    - i. Keep hands and equipment clean
    - ii. Separate raw and cooked food
    - iii. Cook food thoroughly
    - iv. Keep food at safe temperatures
    - v. Use safe water and raw materials
  - Improve animal health: Strengthen the animal health sector to reduce TB prevalence in livestock.
  - Reduce human risk: Identify at-risk populations, such as:
    - i. Communities living closely with livestock, particularly in rural or nomadic areas with limited access to healthcare and safe food.
    - ii. Occupational groups like farmers, veterinarians, abattoir workers, and livestock traders.
    - iii. Children and those consuming unpasteurized dairy products.
    - iv. Immunocompromised individuals, including people with HIV/AIDS.

## Improving Diagnosis of Zoonotic TB

Diagnostic tools need to be expanded to better identify *M. bovis* in humans. Common tests do not distinguish *M. bovis* from *M. tuberculosis*, leading to misclassification. *M. bovis* can be identified by PCR and gene sequencing of culture isolates. Given its natural resistance to pyrazinamide, drug susceptibility testing should be expanded to ensure proper treatment for zoonotic TB patients.

## **CHAPTER 3: TUBERCULOSIS SCREENING AND DIAGNOSIS**

### **TB SCREENING**

TB screening is essential for timely diagnosis and treatment. It involves systematically identifying individuals within specific populations at high risk for TB disease. This typically includes a rapid assessment using screening tests or examinations to efficiently distinguish those with a high probability of having TB from those who are unlikely. For individuals with a positive screening result, a thorough diagnostic evaluation is crucial, combining diagnostic tests and clinical assessment to confirm the presence of active TB disease.

TB screening ensures:

1. TB disease is detected early and treatment is initiated promptly, with the ultimate aim of reducing the risk of poor treatment outcomes, health sequelae and the adverse social and economic consequences of TB
2. Reduction in the community-level prevalence of TB disease, thus reducing transmission of *Mycobacterium tuberculosis*
3. Identification of individuals who are eligible for and would benefit from TB preventive treatment (TPT) once TB disease is ruled out, thus further averting future incident TB

Screening should be conducted using the most sensitive and most specific screening algorithm possible, with a screening test (e.g., Chest Xray) that identifies those with a higher likelihood of having TB and a diagnostic test to confirm the diagnosis.

### **People to prioritise for TB screening**

There are individuals who have increased risk of TB and when diagnosed with TB, have a higher likelihood of poor outcomes. Such individuals should be prioritised for systematic TB screening.

- i.Individuals in areas where the TB prevalence is high. The risk of TB is increased for individuals in areas where the TB prevalence is high (hotspots). Hotspots should be mapped and individuals in these areas screened.
- ii.People with structural risk factors. Individuals with structural risk factors for TB are those that are at an increased risk of TB and of poor health outcomes from TB due to structural determinants e.g., poverty, malnutrition, overcrowding, poor living conditions.
- iii.Key and vulnerable populations such as individuals with high risk for TB or have limited or no access to health care. These populations include: slum dwellers, adolescents, mobile populations (pastoralists, truckers, taxi drivers, fisher folks, sex workers), elderly persons, refugees/asylum seekers/displaced persons/migrants, miners, PLHIV, smokers, alcohol and drug abusers.
- iv.People living with HIV. People living with HIV (PLHIV) should be systematically screened for TB disease at each visit to a health facility, as they are approximately 19 times more likely to develop TB disease than those without HIV.
- v.Household or close contacts. Contact screening should always be done when a person with TB has any of the following characteristics: bacteriologically confirmed pulmonary TB, proven or presumed multidrug-resistant TB or extensively drug-resistant TB, a person living with HIV or a child younger than 5 years.
- vi.Prisoners and people in penitentiary institutions. The estimated incidence of TB among people residing in prisons is 23 times higher than that among the general population. Systematic screening for TB disease should thus be conducted in prisons and penitentiary institutions. At a minimum,

screening in prisons and other penitentiary institutions should always include screening when a person enters a detention facility, annual screening and screening upon release to prevent the reintroduction of TB into the broader community.

vii. People attending health care services with risk factors for TB. Patients seeking care at health facilities with risk factors for TB should all be screened for TB. The risk factors are summarised in Table 3 below.

*Table 3 Risk factors for tuberculosis (TB) to be considered when prioritizing TB screening among people attending health care facilities*

Risk factor	Risk of TB or poor outcomes
Fibrotic lesions on chest X-ray	Studies have shown an increased risk of developing TB disease among individuals with fibrotic lesions identified on chest X-ray but who are not diagnosed with TB disease
Diabetes mellitus (DM)	The risk of TB for patients with DM ranges from 1.5 to 3.1, with a decreasing risk in patients with well-controlled DM. Patients with DM are also at an increased risk of relapse, treatment failure and death
Previous TB	Patients with a history of TB are at increased risk of subsequent TB episodes, poor outcomes and developing drug-resistant TB
Chronic lung disease	Risk of TB is increased in certain lung diseases e.g., in COPD the risk of developing TB ranges from 2.5 to 3.0
Smoking	People who smoke or who have a history of smoking have an increased risk of TB. Smokers are also at an increased risk of drug-resistant TB and poor outcomes from TB, including relapse and death
Alcohol use disorder	From systematic reviews, alcohol use and alcohol use disorder increase risks of treatment failure and development of drug-resistant TB. For every 10–20 g of daily alcohol intake, there is a 12% increase in TB risk
Substance use disorder	People with substance use disorder are at increased risks of treatment failure, development of drug resistance, and mortality from TB due to low adherence and coincident clinical, socioeconomic and structural risk factors
Malnourishment	A low BMI and MUAC is associated with an increased risk of TB. There are multiple pathways by which undernourishment can increase the risk of TB, including cell-mediated immunity and micronutrient deficiency.
Pregnancy	The risk of TB is increased in pregnancy and the postpartum period. TB in pregnancy is associated with adverse outcomes and complications during birth. These outcomes include a roughly 2-fold increased risk of premature birth, low birthweight and intrauterine growth retardation, and a 6-fold increased risk of perinatal death
Immunocompromising conditions (organ transplant, renal failure, dialysis)	Patients with immunosuppression for reasons other than HIV have a greatly increased risk of TB
Health care workers	Health care workers have an increased risk of TB disease compared to the general population

**Health care workers are a specific group that merits consideration for screening in health facilities, given the potentially high level of occupational exposure and the risk of further transmission to patients.**

Identifying the population groups that need to be screened and tested is key. A universal standard for this has been defined and includes special considerations for children. All individuals belonging to risk groups for TB should be screened and undergo testing for TB infection.

Uganda undertook a TB key and vulnerable population (KVP) assessment in 2023 to identify priority key and vulnerable populations for TB. Three criteria for identification of KVPs were considered, i.e.,

- People at increased risk of TB
- People with limited access to health services
- People who experience poor outcomes

The KVPs in order of ranking from the assessment is as indicated in Table 4 below.

*Table 4 Key and Vulnerable population (KVP) groups for Uganda*

No.	KVP group	No.	KVP group
1	Slum dwellers	11	Diabetics
2	Adolescents (10 - 19 years)	12	Alcohol and drug abusers
3	Mobile populations (Pastoralists, truckers, taxi drivers, fisher folks, sex workers)	13	TB contacts
4	Elderly persons ( $\geq 60$ years)	14	Children $< 5$ years
5	Refugees and asylum seekers and displaced persons/ Migrants	15	People living with disabilities
6	People living with HIV	16	Uniformed personnel
7	Miners	17	Health care workers
8	Prisoners and detainees	18	Undernourished
9	Men	19	School-going children
10	Smokers		

The slum dwellers live and work in congregate settings which increases their risk of infection. They live in urban underserved areas and suffer from limited access to healthcare facilities. They are likely to discontinue treatment and thus face poor outcomes.

Adolescent and school going children have increased risk due to being exposed to congregate settings, particularly in schools. They have unique needs and most often are dependent on parents, or guardians and school staff such as nurses for their healthcare. They often don't disclose illnesses, which limits their access to timely healthcare services. Current data suggests that they are at risk for poor TB treatment outcomes.

Mobile populations include pastoralists, truckers, taxi drivers, fisher folks and sex workers. Their occupations put them at an increased risk of infection, and coupled with high mobility limits their access to healthcare services. They have high rates of lost to follow up and thus have poor treatment outcomes.

The elderly have weakened immune systems in addition to having other comorbidities that increase their risk of infection and poor treatment outcomes. Age-related financial and physical dependency also limits their access to healthcare services.

## **TB screening tools**

In Uganda, there are several screening tools/tests that should be used to facilitate systematic screening. The TB screening tools/tests are not intended to provide a definitive diagnosis. The screening **tests should be followed by a diagnostic test** which is offered as part of a comprehensive clinical evaluation to confirm or rule out TB disease in individuals who screen positive. These tools/tests include

- i.Symptom screening: This is feasible, easy to implement and low-cost. It is highly acceptable, because it is non-invasive and is a usual part of the clinical assessment of people under care. In Uganda, the intensified case finding (ICF) guide (Figure 6 is used to aid symptom screening).
- ii.Chest X-ray (CXR): This imaging technique is helpful in identifying lung abnormalities. CXR is a good screening tool for pulmonary TB because of its high estimated accuracy for detecting TB disease, even before the onset of symptoms (asymptomatic TB). It has been added onto the ICF guide as part of the screening tools (Figure 6).
- iii.Computer aided diagnostic (CAD) technologies for screening: CAD software packages have been introduced to automate interpretation of digital CXR images for pulmonary TB disease- related abnormalities. CAD products analyse digital CXR images and generate a score that corresponds to an increasing likelihood of TB as the score increases.
- iv.C-reactive protein: CRP is an indicator of general inflammation that can be measured using point-of-care test performed on capillary blood collected via finger prick. CRP is used for screening for active TB in PLHIV who are 10 years and above. CRP can play an important role in ruling out TB disease in ART naïve PLHIV

Figure 5 Intensified Case finding Guide

## TB Screening Guide

**This guide should be administered by either a health care worker or lay provider to identify persons with presumptive TB among individuals seeking care at the health facility or community.**

### STEP 1: The person conducting the assessment asks the following questions:

1	Does the individual have any cough? (assess cough regardless of the duration)	Yes	No
2	Has the individual had persistent fevers for 2 weeks or more?	Yes	No
3	Has the individual had noticeable weight loss (more than 3 kg)	Yes	No
4	Has the individual had excessive night sweats for 3 weeks or more?	Yes	No
5	Has the child had poor weight gain in the last one month? (for children <5 years)	Yes	No
6	Has the child had contact with a person with pulmonary TB? (for children <5yr.)	Yes	No

- Poor weight gain. Very low weight (weight-& less than -3 z-score), or underweight (weight-for + age less than -2 z-score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening, or MUAC measurements: Yellow (moderate malnutrition) or Red (severe malnutrition)

### STEP 2: Guide for Actions to:

Consider presumptive TB

1. If the individual is a high-risk for TB (PLHIV, TB contacts, diabetic patients, malnourished people, miners, prisoners, refugees and health workers) and has current cough, Irrespective of duration.
2. If the individual is not high risk for TB and has persistent cough for 2 weeks or more, or has current cough with any other symptom suggestive of TB
3. If the individual has no cough but has other symptoms suggestive of TB, refer to clinician for further evaluation (detailed history, physical examinations and tests) to ascertain if the person is presumptive TB or not.

Actions to take

1. Separate and direct the individual(s) with cough to a designated area for people with cough
2. Obtain sputum sample from every presumptive TB client for a diagnostic test with a mWRD.
3. For children who cannot produce sputum, consider stool sample for Xpert MTB/RIF Ultra test
4. Fast-track to see a clinician for further clinical assessment and investigations. If no to all questions: repeat TB assessment at subsequent visits

### STEP 3: Record of Information at Health facility level

1. Document the screening action in the relevant health facility records at each care entry point e.g., OPD, In-patients ward, MCH, integrated nutrition register, etc.
2. In the HIV/ART clinics, record the information in the comprehensive ART card; and then transfer to the Pre ART or ART register
3. If the individual is presumed with TB, record the information in a presumptive TB register.

*Revised July 2024*

## **TB Screening Algorithms**

An algorithm for systematic TB screening should combine one or several screening tests and a separate diagnostic evaluation for TB disease. These include:

1. **Serial screening algorithms:** These comprise two screening tests conducted successively, with referral for a second screening test according to the results of the first test. The serial algorithms could be further divided into:

- **Sequential positive serial screening algorithm:** This is one in which a positive result on the first test requires referral to a second screening test, followed by diagnostic evaluation of those who screen positive on both screening tests e.g., individuals who have a positive screen using symptoms are further screened with CXR and those who are positive on CXR undergo diagnostic evaluation.
- **Sequential negative serial screening algorithm:** This is one in which a positive or abnormal result on the first screening test results is referral to diagnostic evaluation

A negative or normal result on the first screening test results is referred for a second screening test and then subsequent referral for diagnostic evaluation for those who screen positive or abnormal in the second screening test e.g., all individuals who have a positive screen on symptoms are referred for diagnostic evaluation while those with a negative screen are further screened with a CXR and those that are positive on the CXR undergo diagnostic evaluation.

2. **Parallel screening algorithms:** Here, screening tests are conducted at the same time and individuals who screen positive on either or both tests are referred for diagnostic evaluation e.g., doing symptoms screening at the same time with a Chest X-ray.

TB screening could be done at the health facility or in the community.

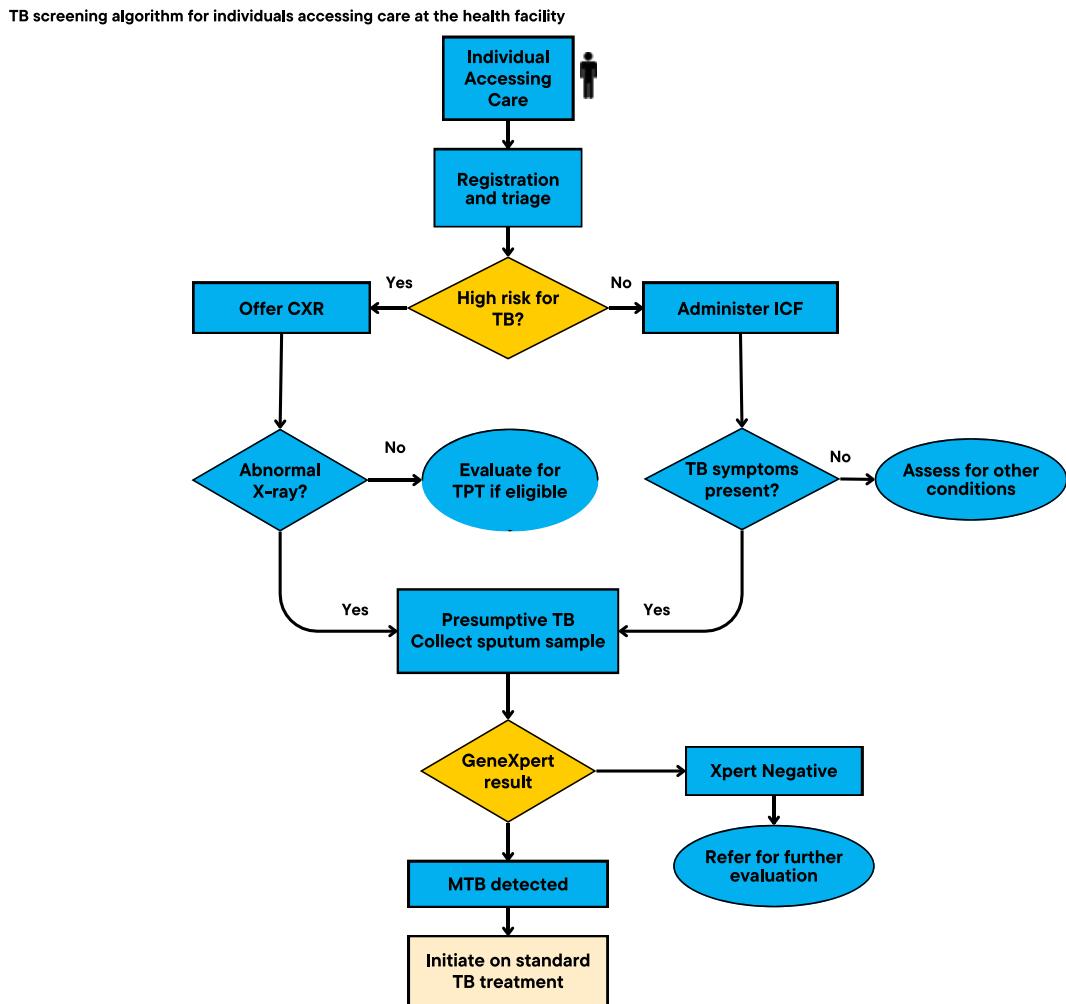
### **i. Health facility-based TB screening**

The NTLP has adopted a modified parallel screening approach whereby all individuals seeking care are screened with both symptoms (ICF guide) and CXR where available. Individuals who screen positive on either or both tests are referred for diagnostic evaluation using the GeneXpert Ultra or any other method available.

CXR is prioritised for individuals at high risk for TB. These include PLHIV, contacts of TB patients, diabetic patients, people with malnutrition, prisoners, refugees, health workers, etc.

**Note:** CXR should be offered once in 12 months, unless otherwise indicated.

Figure 6 TB screening algorithm for all individuals at the health facility



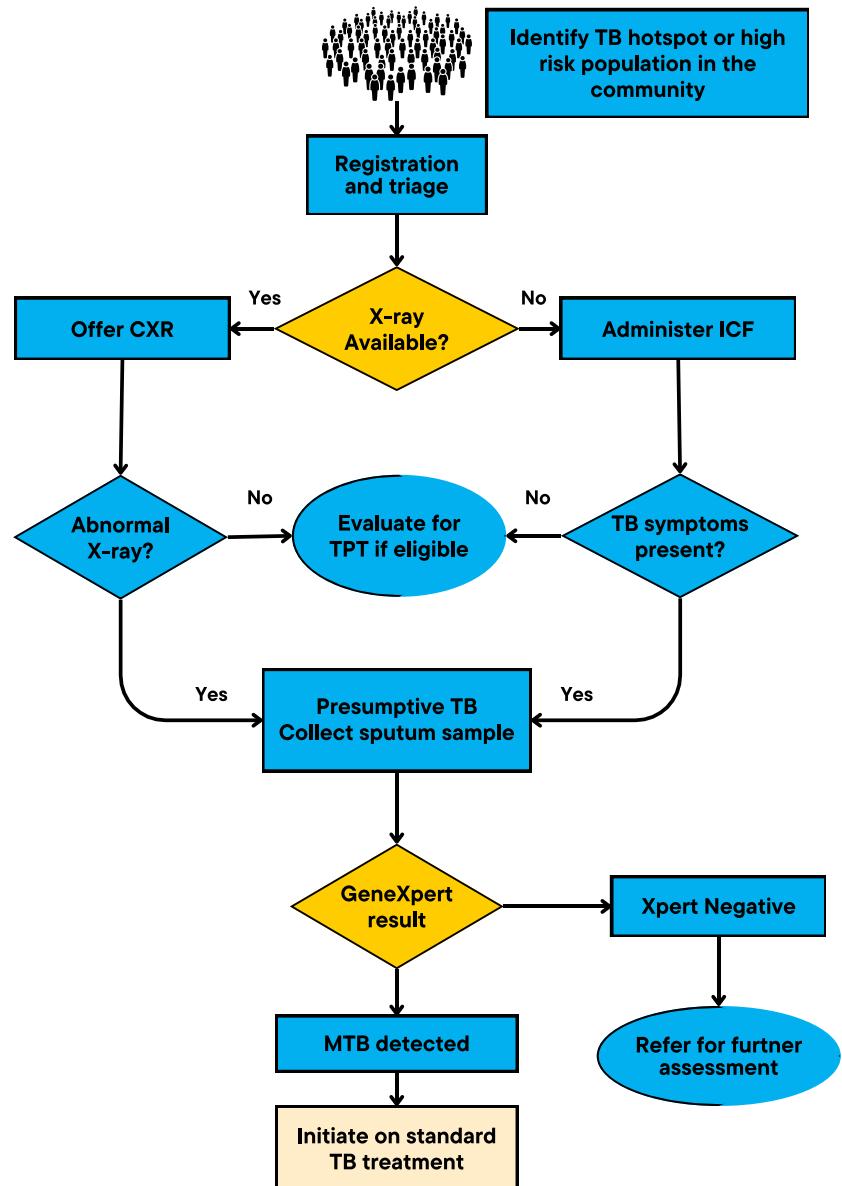
1. For TB screening in the community, target hotspots (areas with high TB prevalence) e.g., urban slums, taxi/ bus parks, refugee camps, prisons, landing sites, etc.)
2. High-risk individuals for TB include: PLHIV, TB contacts, diabetic patients, malnourished persons, prisoners, refugees, smokers, health workers, mentally ill persons, fisher-folks, slum dwellers, and mobile populations.
3. Eligible for CXR: prioritize all individuals at high-risk for TB for screening with CXR
  - If eligible, offer CXR examination at baseline or first visit and repeat after 12 months.
  - In children, offer CXR screening only for those who are contacts of TB patients.
  - Individuals who had recent X-ray examination (less than a year) should not be offered an X-ray exam

## ii. Community based screening

In the community, screening should be done through routine or targeted screening in areas where the prevalence of TB is high (hotspots), identified using surveillance data (e.g. electronic case-based surveillance system, Geospatial mapping, etc.) For targeted community-based screening (i.e., hot spot screening), the use of the Chest X-ray is encouraged. The chest X-ray option includes mobile digital X-ray (mobile clinics & portable digital X-ray). In instances where a Chest X-ray is not available, symptom-based screening should be used.

Figure 7 Community screening algorithm

TB screening algorithm for individuals in the community



1. For TB screening in the community, target hotspots (areas with high TB prevalence) e.g., urban slums, taxi/ bus parks, refugee camps, prisons, landing sites, etc.)
2. High-risk individuals for TB include: PLHIV, TB contacts, diabetic patients, malnourished persons, prisoners, refugees, smokers, health workers, mentally ill persons, fisher-folks, slum dwellers, and mobile populations.
3. Eligible for CXR: prioritize all individuals at high-risk for TB for screening with CXR
  - If eligible, offer CXR examination at baseline or first visit and repeat after 12 months.
  - In children, offer CXR screening only for those who are contacts of TB patients.
  - Individuals who had recent X-ray examination (less than a year) should not be offered an X-ray exam

## 3.2 TB DIAGNOSIS

### Laboratory Diagnostic methods

Laboratory confirmation of TB and drug resistance is essential to ensure individuals with TB are correctly diagnosed and have access to appropriate treatment as soon as possible. All presumptive TB patients should be examined per the standardized procedures and national algorithms. In Uganda, the following diagnostic tests are used to confirm/exclude TB:

1. Smear Microscopy
2. Xpert MTB/RIF Ultra
3. Xpert MTB/XDR assay
4. Truenat (MTB plus test and MTB RIF Dx Test)
5. Loop Mediated Isothermal Amplification assay (TB-LAMP)
6. Lateral flow Lipoarabinomannan assay (LF-LAM)
7. Culture (solid and liquid) Phenotypic drug susceptibility testing (LJ-DST or MGIT-DST)
8. Line-probe assays (LPAs)
9. Targeted Next Generation Sequencing
10. Histopathology

### Laboratory diagnosis

All efforts should be made to make a laboratory confirmation of TB diagnosis in all patients with presumptive TB identified through the screening process (refer to chapter 3). This is important for clinical monitoring of treatment response. It is also important for TB reporting and monitoring of TB control efforts. However, a clinician can still make a diagnosis of TB even in the absence of confirmatory laboratory confirmation. Several investigations and tests can be deployed to aid the diagnosis of TB. These are described below:

#### Bacteriological

##### Microscopic examination of sputum smears

Sputum microscopy remains the widely used method of identifying patients with infectious forms of pulmonary TB. Microscopy is easy to perform at the peripheral laboratories and is cheap. Sputum-smear microscopy is a relatively insensitive test, with a limit of detection (LoD) of 5,000– 10,000 bacilli per millilitre of sputum. Furthermore, sputum-smear microscopy cannot distinguish drug-susceptible strains from drug-resistant strains.

Microscopy method is used for TB diagnosis, and a key tool for monitoring patient response to treatment. The light microscope and Ziehl– Neelsen staining (Figure 9) have been in use for more than a century. Light microscopy has a good specificity but variable and low sensitivity in children and in HIV-infected TB patients. To improve sensitivity of light microscopy, sputum concentration methods have been developed. Concentration methods improve ZN yield by 13% and should be encouraged where appropriate. However, this approach can only be performed at relatively well-equipped laboratories; where there is culture facilities hence limiting its usefulness in peripheral clinics where the need is highest.

Fluorescent Microscopy (FM) (Figure 10) is an improvement on the light microscopy (Figure 9). FM has demonstrated to be superior to light microscopy (ZN). However, the cost and need for electricity has led to limited application of fluorescent microscopy.

A new fluorescent microscopy that uses Light Emitting Diodes (LED) which can use ordinary batteries and do not need the use of a dark room has been developed (WHO, 2010). The LED has a sensitivity comparable to that of standard FM and is cheaper.

Figure 9 Positive Ziehl Neelsen smear

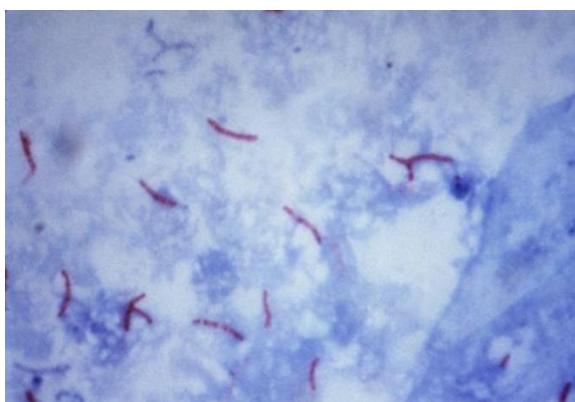


Figure 9 Positive fluorescent microscopy



#### 3.2.2.1.2 Nucleic Acid Amplification Tests (NAAT):

WHO recommends that TB programmes transition to replacing microscopy as the initial diagnostic test with molecular WHO approved rapid diagnostic tests (mWRDs). Nucleic Acid Amplification tests (NAAT) are based on the principle of detecting and amplifying (making more copies of) the M. tb genetic material. They are also known as molecular tests, and several of these have been developed to aid in TB diagnosis. The newer, rapid and sensitive molecular tests recommended for the initial detection of M. tb and drug resistance are designated as mWRDs; and include Xpert MTB/RIF Ultra, Truenat MTB Plus, and Truenat MTB-RIF Dx tests and loop-mediated isothermal amplification (TB-LAMP).

##### i. Xpert MTB/RIF Ultra

The Xpert MTB/RIF Ultra assay (also called Xpert Ultra) is currently the most used NAAT in Uganda. It's an automated DNA test for mycobacteria specific for M.tb (IS6110) and for the mutation that causes resistance to Rifampicin (rpoB). Several samples can be used for the Xpert MTB/RIF Ultra. These include: Sputum, lymph node tissue and aspirates, pleural fluid, cerebrospinal fluid, gastric aspirates and stool. Results can be expected in less than 2 hours.

*Table 5 Xpert MTB/RIF Ultra results and their interpretation*

<b>Result</b>	<b>Interpretation and action</b>
MTB detected RIF resistance NOT detected	Start or continue patient on first line TB treatment
MTB detected RIF resistance detected	Refer patient for DR/ MDR-TB treatment Send another sample to NTRL for DST (a sample should be sent by the DR-TB treatment initiation site)
If MTB detected RIF resistance indeterminate	Start first line TB treatment Repeat test using another sample. If RR, refer for MDR-TB treatment Refer sample for culture, 1st & 2nd line DST
MTB TRACE Detected, Rifampicin Resistance Indeterminate ("trace calls")	Start treatment with first line TB treatment Another sample should be sent to NTRL for culture and DST.
MTB NOT detected	Conduct clinical evaluation or treatment according to the national diagnostic algorithm
Error, invalid or no result	For error or no results repeat test with a new cartridge For invalid results repeat the test with another sample and a new cartridge

At very low bacterial loads, Xpert Ultra can give a "trace" result, which is not based on amplification of the rpoB target and therefore does not give results for RIF susceptibility or resistance

## **ii.Xpert MTB/XDR**

Xpert® MTB/XDR test is designed to detect pre-extensively drug resistant (pre-XDR) TB. The test is performed on 10 colour module GeneXpert ® Systems and is intended for use as a reflex test for a specimen (unprocessed sputum, concentrated sputum sediments, or MGIT culture) that is determined to be MTB positive. In Uganda the Xpert MTB/XDR test is currently prioritised for patients with MTB positive and Rifampicin resistance. It can provide results within approximately 90 minutes. When MTB is detected, the Xpert® MTB/XDR test can also detect:

- Isoniazid (INH) resistance associated mutations in the katG and fabG1 genes, oxyR-ahpC intergenic region and inhA promoter
- Ethionamide (ETH) resistance associated with inhA promoter mutations only
- Fluoroquinolone (FLQ) resistance associated mutations in the gyrA and gyrB quinolone resistance determining regions (QRDR)

**In addition to sputum sample, a stool sample should be used for TB testing in children. The right procedures for stool sample processing using simple-one-step stool processing method should be followed**

Table 6 Xpert MTB/XDR results and their interpretation

Results	Interpretation and decisions
Invalid/Error/No result	Perform a 2 <sup>nd</sup> test on a new specimen
MTB detected; No resistance detected	Treat according to the result of Xpert MTB/RIF Ultra. Resistance cannot be ruled out because other resistance-conferring mutations are not detected by Xpert MTB/XDR (e.g., only 30% of Eto resistance conferring mutations are detected). Perform phenotypic DST (pDST) for resistance to other TB drugs and monitor treatment
MTB detected; Low INH resistance detected  INH resistance detected  Low FLQ resistance detected  FLQ resistance detected  ETH resistance detected  AMK, KAN and/or CAP resistance detected	Evaluate risk factors of resistance for each drug High risk of resistance: consider as resistant to the drug. If low-level H resistance detected (inhA mutation and no katG mutation): Hh can be used, but not counted as a likely effective drug. If low-level resistance to FQs detected: Mfx can be used, but not counted as a likely effective drug Resistance to Eto can be detected (inhA mutation). However, a negative result does not rule out resistance. Perform DST for resistance to other TB drugs and monitor treatment. Low risk of resistance (f): perform a 2 <sup>nd</sup> test on a new specimen (g). If the 2nd test shows: Drug susceptibility: treat with the drug Drug resistance: consider as resistant (see above for "High risk of resistance to the drug").
MTB detected; Drug resistance indeterminate	Perform a 2nd test on a new specimen. If still "indeterminate": treat with likely effective drug(s) while investigating resistance with pDST or other gDST (second-line LPA, genome sequencing).

### iii. Truenat

The Truenat testing system uses portable, battery-operated devices to rapidly detect *Mycobacterium tuberculosis* complex bacteria (MTBC) and rifampicin resistance. The system is designed to be operated in peripheral laboratories with minimal infrastructure and is therefore considered to be the first molecular near-point-of-care test for TB recommended by the World Health Organization (WHO). Truenat is a two-step test. The first test being Truenat MTB Plus which detects MTB and if MTB Plus test is positive, an aliquot of already extracted DNA is loaded on to MTB Rif chip to test for rifampicin resistance.

### iv. TB-LAMP assay

The TB-LAMP assay is designed to detect MTB directly from sputum specimens. This is a manual assay and provides results in less than 2 hours. It does not require sophisticated instrumentation and can be used at the peripheral health centre level given the biosafety requirements are similar to those for sputum-smear microscopy. TB-LAMP does not detect resistance to anti-TB drugs.

Where available, TB-LAMP should be used in place of sputum-smear microscopy for diagnosing pulmonary TB in adults with signs and symptoms consistent with TB because it is more superior to microscopy (offers easy visual result interpretation with a throughput of 14 samples per run).

### v. Line Probe Assay

The LPA test is another molecular test that allows for rapid detection of drug resistance to first and second line agents. The LPA test is a DNA strip based test.

First-line LPAs (FL-LPAs) allow the detection of resistance to Rifampicin (R) and Isoniazid (INH) and are recommended for patients in whom a rapid confirmation of MDR status is needed. Second-line LPAs (SL-LPAs) allow the detection of resistance to fluoroquinolones (FQs) and second line injectable drugs (kanamycin, amikacin, capreomycin).

LPAs can be used for testing of culture isolates (indirect testing), as well as direct testing of AFB smear microscopy positive specimens (FL-LPA), and both smear positive and smear negative sputum specimens (SL-LPA). Like Xpert MTB/RIF, LPA returns the following results: MTB detected or MTB not detected. MTB not detected does not completely rule out TB. It gives an indication of the minimum inhibitory concentration (MIC) as well.

The first line Probe assay report could be as follows:<sup>2</sup>

- a) Rifampicin: Resistance inferred
- b) Rifampicin: Resistance detected
- c) Isoniazid: Mutation associated with high level increase in MIC detected
- d) Isoniazid: Mutation associated with at least low-level increase in MIC detected
- e) Isoniazid: Mutation likely associated with at least low-level increase in MIC detected
- f) Isoniazid: Mutation likely associated with at least low-level increase in MIC inferred

The report could also give an indication of the resistance profile for the second line drugs. Possible second line reports could take the following forms:

*Table 7 Types of Second line reports*

Resistance not detected
Levofloxacin: Resistance detected, Moxifloxacin: Mutation associated with high level increase in MIC for Mfx detected
Levofloxacin: Resistance detected, Moxifloxacin: Mutation associated with at least low-level increase in MIC for Mfx detected
Levofloxacin: Resistance inferred, Moxifloxacin: Mutation associated with at least low-level increase in MIC for Mfx inferred
Amikacin: Resistance detected, Kanamycin: Resistance detected, Capreomycin: Resistance detected
Amikacin: Resistance not detected, Kanamycin: Resistance detected, Capreomycin: Resistance not detected
Amikacin: Resistance inferred, Kanamycin: Resistance inferred, Capreomycin: Resistance inferred
Amikacin: Resistance not detected, Kanamycin: Resistance inferred, Capreomycin: Resistance not detected

## Culture

A culture test is an invitro test which involves studying bacteria by growing the bacteria on solid or liquid media which supports growth. This is to find out if particular bacteria are present. In the case of the TB culture test, the test ascertains if the TB bacteria (*Mycobacterium tuberculosis*) are present. See more at: <http://www.tbfacts.org/culture-tb/#sthash.YFcLUfu1.dpuf>

The probability of finding AFB in sputum specimens by smear microscopy or molecular tests is directly related to the concentration of bacilli in the sputum. In comparison, mycobacterial culture can detect far lower numbers of TB bacilli. Moreover, the culture makes it possible to identify the mycobacterial species based on biochemical and other properties. Culture can be done using both the solid LJ media and liquid MGIT 960 media. It is done in specialized laboratories for example the NTRL. All clinical samples can be cultured.

<sup>2</sup> <https://www.who.int/publications/i/item/9789240046665>

Culture of *M. tb* bacilli is very sensitive and specific, but is expensive, as it is a complex and sophisticated procedure. It requires a specialized laboratory set-up, and culture results are available only after 6 to 8 weeks. Culture with DST takes even longer. If available, culture can be used for diagnosis or confirmation of the diagnosis of TB in patients with PTB and EPTB. Since it is more sensitive than smear, culture may also have a role in the diagnosis of smear-negative, HIV-positive TB suspects who are likely to be paucibacillary.

### **Antigen tests**

**TB LAM test:** This is an immunocapture assay based on the detection of mycobacterial lipoarabinomannan (LAM) in urine. It is a potential point of care test for certain populations being evaluated for TB. The detection of mycobacterial LAM antigen in urine does not provide any information on drug resistance.

The lateral flow urine lipoarabinomannan assay (Urine TB LAM) should be used as the preferred initial test for TB diagnosis among PLHIV, followed by mWRD such as GeneXpert, TRUENAT or TBLAMP, or microscopy in PLHIV that are:

- With advanced HIV disease or
- Who are seriously ill irrespective of signs and symptoms of TB and CD4 cell count or
- With unsuppressed viral load (i.e., VL > 1000 copies/ml of blood)

#### **Note:**

1. TB LAM MUST NOT be used for HIV NEGATIVE patients
2. The above national recommendations apply to both in-patient and out-patient settings
3. Whereas children less than 5 years who are new and have been on ART for less than one year are all considered to have AHD, they will only be eligible for a TB LAM test if they have AHD symptoms and signs (refer to the symptom screen and advanced disease management pathway).

Regardless of TB LAM results, a sputum sample should be collected and sent for mWRD (such as Gene Xpert, TRUENAT, TB-LAMP) for simultaneous detection of *M. tuberculosis* and Rifampicin resistance. All PLHIVs with a positive TB LAM should be classified as Bacteriologically confirmed pulmonary TB patients (P-BC) and promptly started on TB treatment. Treatment monitoring for all TB LAM positive PLHIVs should be done by microscopy using a sputum sample.

**“Seriously ill”** is defined based on 4 danger signs: respiratory rate > 30 breaths/min, temperature > 39°C, heart rate > 120 beats/min and unable to walk unaided.

**In children**, the signs include: lethargy, convulsions, inability to feed, repeated vomiting, temperature > 39°C and tachycardia/tachypnoea.

## **Next Generation Sequencing (NGS) / target- New Generation Sequencing (tNGS)**

NGS provides an opportunity to expand access to TB drug-resistance testing. Presently there are no mWRDs that detect resistance to new and repurposed drugs such as Bedaquiline, linezolid, delamanid and Pretomanid. Also the current mWRDs only detect resistance to a limited number of drugs and cover only a single or few resistance-associated gene regions. NGS technology involves amplifying selected genes to detect resistance to many drugs with a single test. In addition, NGS-based tests can detect resistance to new and repurposed drugs not currently included in any other molecular assays.

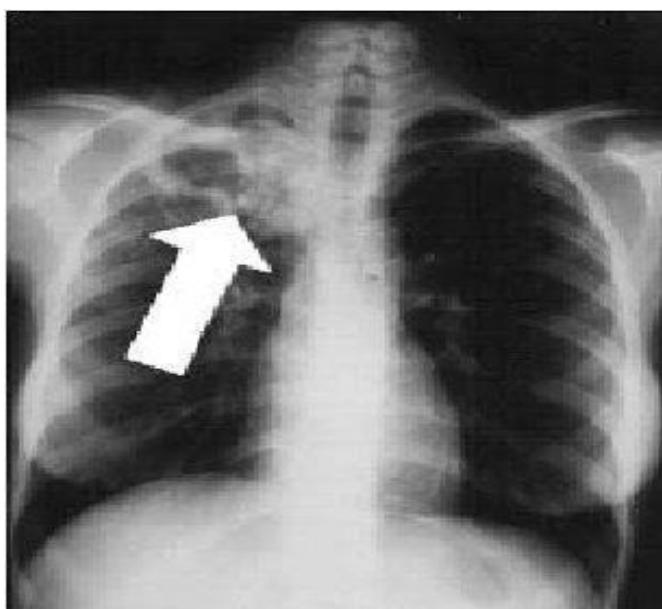
Available WHO evidence supports the use of tNGS to detect drug resistance after TB diagnosis, to guide clinical decision-making for DR-TB treatment. tNGS does not replace mWRDs that are more accessible, cheaper and easier to perform for detecting resistance to rifampicin, isoniazid and fluoroquinolones. However, tNGS can be considered an alternative for prioritized patient populations requiring comprehensive DST with faster results compared with phenotypic DST, or where access to phenotypic DST is limited. Although tNGS could provide important early DST results, which may impact treatment decisions in some patients, the suboptimal sensitivity for selected new and repurposed drugs implies that phenotypic DST is still required. However, the uptake of NGS/tNGS for DR-TB diagnosis is currently hindered by costs and challenges in integration into the existing laboratory workflow and algorithms.

## **Radiology**

### **X-ray**

Radiology investigations such as Chest X-ray can be used to support a diagnosis of TB. Features of Chest X-ray consistent with TB disease include cavitation (Figure 11), milliary picture (Figure 12), pleural effusion, mediastinal and hilar lymph node enlargement with or without lung infiltration. Although the findings of radiology are nonspecific, abnormalities like any heterogeneous opacities and cavitation if located in the upper parts of the lung are more likely to be caused by TB. The CXR has a dual role i.e., can be used both as a screening test (refer to screening section) or diagnostic investigation

*Figure 11 Cavitory pattern of TB*



*Figure 11 Milliary pattern of TB*



Figure 12 Abdominal Ultrasound showing mesenteric lymphadenopathy



### Histological examination

Pathology can play a complementary role in confirming the diagnosis of EPTB, such as TB lymphadenitis. Multiplication of tubercle bacilli in any site of the human body causes a specific type of inflammation, with formation of characteristic granuloma that can be found on histology.

Samples can be taken in the following ways:

- i.Fine needle aspiration of the lymph nodes: affected peripheral lymph nodes, particularly cervical nodes, can be aspirated.
- ii.Tissue biopsy: serous membranes (pleura, pericardium and peritoneum), skin, lymph node, endometrium, bronchial mucosa or liver tissue can be taken, with an appropriate instrument or during surgery, the latter being useful in getting biopsies from deep organs.

### TUBERCULOSIS DIAGNOSTIC ALGORITHMS

Effective diagnostic algorithms are crucial for ensuring accurate and rapid TB diagnosis, enabling timely initiation of appropriate treatment to improve outcomes, reduce transmission, and prevent drug resistance. The diagnostic pathway starts with a positive TB screening result (see Chapter 3 for detailed screening algorithms).

**Presumptive TB patients may not always present with symptoms that match the latest screening guideline recommendations, but still have an increased probability for TB disease requiring diagnostic testing**

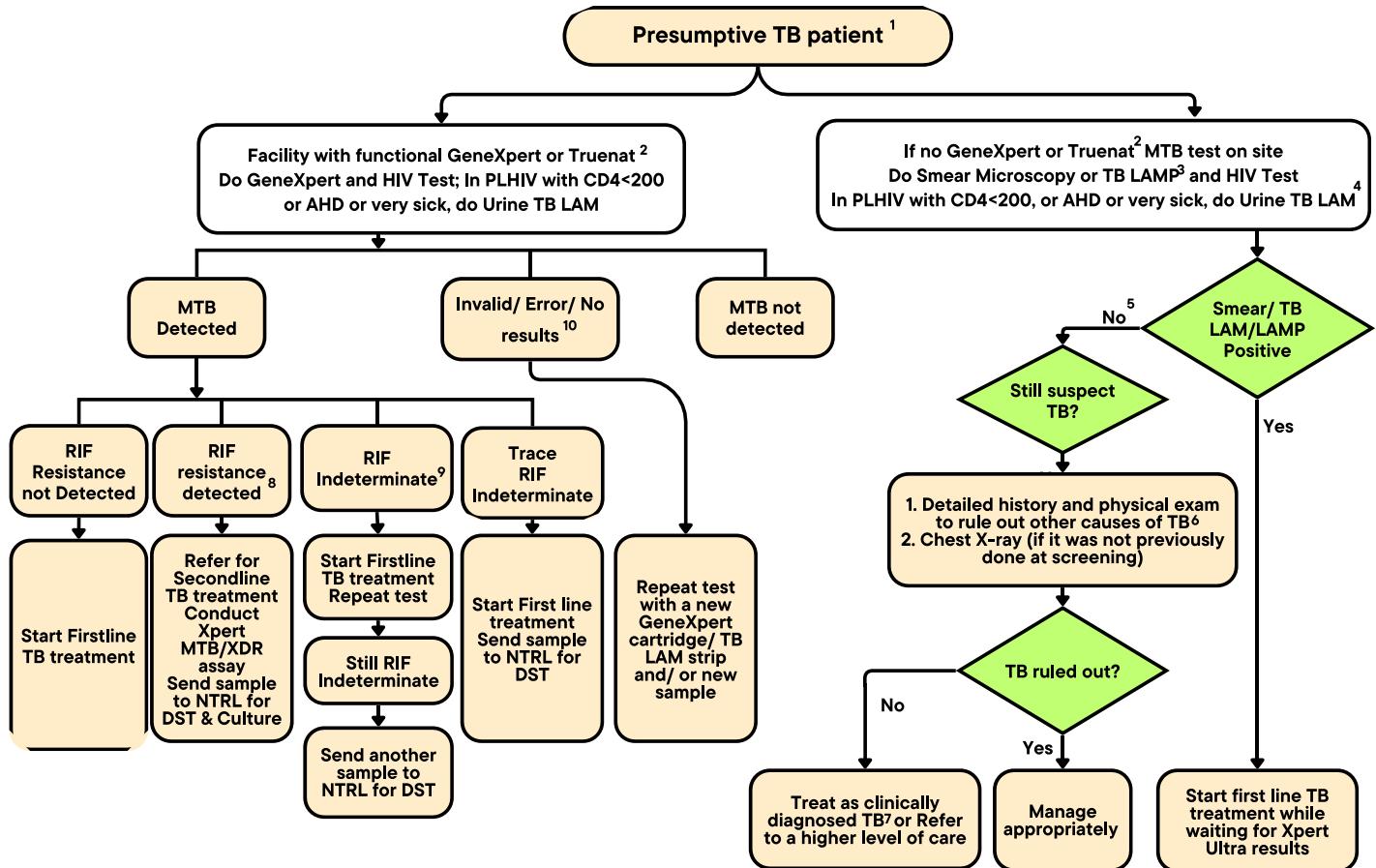
GeneXpert, Truenat, or TB LAMP should be used as the initial diagnostic test for TB presumptive patients. Where these are unavailable, fluorescent microscopy is recommended, with sputum samples sent to a GeneXpert facility for TB and Rifampicin resistance testing. Patients with positive smears should begin TB treatment while awaiting resistance results.

**GeneXpert/Truenat/TB LAMP should be used as the initial diagnostic for TB among the presumptive TB patients**

If Rifampicin resistance is confirmed, they should be referred for second-line treatment at a designated drug-resistant TB facility.

PLHIV who qualify for TB-LAM should have GeneXpert to ascertain the rifampicin resistance status. The algorithm as is indicated in Figure 14 below:

Figure 13 Algorithm for diagnosis and initiation of tuberculosis treatment (Version 1, 26th September 2024)



1. Presumptive TB is presence of any or a combination of the following symptoms; cough≥ 2weeks or current cough with any other TB symptom, fever, night sweats, history of contact with a TB case, weight loss or poor weight gain for children. Also consider abnormal chest x-ray in a high-risk patient as presumptive TB
2. Truenat is a molecular test for diagnosis of TB and Rifampicin resistance
3. TB LAMP Positive- Only Positive TB-LAMP should be sent for Xpert testing. Smear positive (AFB positive): is defined as at least one positive smear
4. Urine TB LAM test should be offered to HIV positive individuals with CD4 ≤ 200 (AHD) or very sick (Temperature >39°C, Respiratory Rate >30 breaths/min, Heart Rate >120 beats/min, New Seizure, Unable to walk without assistance / Bed-ridden). If Urine TB LAM is positive, the Patient should be started on TB Treatment and a sputum sample should be collected for Genexpert testing to rule out Rifampicin resistance.
5. Smear negative: defined as at least one negative smear. Carry out other investigations such as CXR if available. Those with CXR suggestive of TB should be treated as clinically diagnosed TB. If not available or CXR not suggestive, do further history, physical examination and other investigations to exclude other causes of chronic cough, fever and weight loss.
6. Differential Diagnoses of TB: Chronic Obstructive Pulmonary Disease (COPD), heart disease, asthma, bronchiectasis, emphysema; Histoplasma pneumonia, trypanosomiasis, brucellosis; Fungal infection of the lung; Malignancy (lung cancer, lymphoma etc.)
7. TB based on abnormal X-ray suggestive of TB: Features include heterogeneous opacities and cavitation in the upper parts of the lung, mediastinal L/nodes, pleural effusion and miliary picture
8. If MTB detected RIF resistance detected, Refer patient for MDR-TB treatment. Conduct Xpert MTB/XDR assay. Send another sample to NTRL for culture and DST (Sample should be sent by DR-TB treatment initiation site).
9. If MTB detected Rifampicin Resistance Indeterminate; Start first line TB treatment, Repeat Test using another sample. If still indeterminate, send another sample to NTRL for DST.
10. If Error/No result on Xpert, repeat the test with a new cartridge. If Invalid on Xpert, repeat the test with a new sample and new cartridge. For Truenat, repeat the test and follow algorithm to interpret. If both Truenat tests give indeterminate, treat with 1st line TB regimen and promptly conduct additional investigations to assess resistance to rifampicin e.g., DST. Review treatment based on DST result

## TB CASE DEFINITIONS

Once a diagnosis of TB has been made in a patient, it is important that a definition is assigned to them. Case definitions are important for standardizing the process of data collection (case registration) and case notification (unit TB register) and TB reporting requirements to allow for cohort analysis of treatment outcomes. The standard TB case definitions are shown in *Table 8*.

*Table 8 Standard TB case definitions*

Case definition	Description
Presumptive TB patient	Any patient who presents with symptoms and signs suggestive of TB and/or Chest X-ray findings suggestive of TB (previously called a TB suspect).
Bacteriologically confirmed TB patient	A bacteriologically confirmed TB patient is one from whom a biological specimen is positive by smear microscopy, culture, Nucleic Acid Amplification Tests e.g., X-pert MTB/RIF Ultra or WHO recommended new diagnostics. All such cases should be recorded in the unit TB register and notified, regardless of whether TB treatment has been started.
Clinically diagnosed TB patient	A clinically diagnosed TB patient is one who does not fulfil 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

## Classification of TB patients

Four factors determine the classification: the site of the disease (body organ involved), drug resistance, HIV status and the patient's history of previous treatment.

### i. Classification based on site of the disease

The description below applies to all patients irrespective of HIV status.

- **Pulmonary tuberculosis (PTB):** Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra-pulmonary TB.
- **Extra-pulmonary tuberculosis (EPTB):** Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints bones, and meninges.

**Note:** For a presumptive TB patient to be treated as a TB patient, s/he must first be declared a TB patient and a decision is made to treat him/her for TB. A TB patient is what is referred to as a case of TB. However not all TB patients have the same classification. It is this process of classifying the different types of TB patients that is called Case definition

## **ii.Previously treated TB patients**

These are patients who have received one month or more of anti TB drugs in the past. They are sub classified as follows:

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

***NB: New and relapse cases of TB are incident TB cases***

## **iii.Classification based on HIV infection status**

- **HIV-positive TB patient** refers to 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-antiretroviral therapy (ART) register or in the ART register once ART has been started.
- **HIV-negative TB patient** refers to 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** refers to 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.

## **iv.Classification based on drug resistance**

Cases are classified in categories based on drug susceptibility testing (DST) of clinical isolates confirmed to be M. tb: Refer to DR TB section

## CHAPTER 4: TREATMENT OF TUBERCULOSIS

This chapter covers the treatment of confirmed TB (drug-sensitive and drug-resistant), latent TB infection (LTBI), and treatment support, along with TB management in communities, border points, and mortality surveillance. The goal of TB treatment is to cure the disease, prevent transmission, avoid drug resistance, and mitigate post-TB lung disease. Patients must take TB medicines in the correct doses as prescribed, even if they feel well, and complete the full treatment duration to avoid resistance, treatment failure, and death. Prompt initiation of treatment per NTLP guidelines is crucial for stopping TB transmission and achieving better patient outcomes.

The aims of treatment are to:

- i.Cure the TB patient
- ii.Prevent complications and death from TB disease
- iii.Reduce TB transmission
- iv.Prevent development of drug-resistant TB
- v.Prevent post TB lung disease

### ANTI-TB MEDICINES

TB treatment includes first-line medicines for drug-susceptible TB and second-line medicines for drug-resistant TB. The standard abbreviations for first-line anti-TB medicines are listed below and detailed in Table. 9.

*Table 9 Characteristics of First-line anti-tuberculosis medicines*

Drug	Adult dose*	Route†	Common side effects	Contraindications	Important drug interactions
Isoniazid (H)	10mg/kg body wt.(max.300mg)	Oral	Hepatitis, peripheral neuropathy	Active liver disease, known hypersensitivity	Stavudine, Phenytoin, Carbamazepine
Rifampicin (R)	10mg/kg body wt.(max.600mg)	Oral	Flu like syndrome, dermatitis, hepatitis, reddish-brown coloration of urine	Hepatic dysfunction, hypersensitivity to rifamycins	Oral contraceptives, Nevirapine, Warfarin, Phenytoin, Glibenclamide
Pyrazinamide (Z)	30–40 mg/kg daily body wt. (max dose 2500 mg)	Oral	Joint pains, hepatitis	Hepatic impairment known hypersensitivity	None
Ethambutol (E)	15mg/kg body wt.	Oral	Impaired visual acuity and colour vision	Pre-existing optic neuritis, established kidney failure	None
Rifabutin (Rfb)	300mg once daily	Oral	Skin and body fluid discoloration, bone marrow suppression, skin allergies, hepatitis, severe headache, muscle aches, joint pains, visual disturbances	Hypersensitivity to rifamycins, limited data on risk during pregnancy (adverse effects have been seen in animal studies)	NRTIs (Abacavir, Lamivudine, Zidovudine), Efavirenz, Nevirapine, protease inhibitors, integrase inhibitors
Rifapentine (P)	600mg twice weekly	Oral	Skin allergies; fever; jaundice; elevated liver enzymes; irregular heartbeat; gastrointestinal upset and distress; neutropenia	Limited data on risk during pregnancy (damage to foetus was seen in animal studies; bleeding in infant and mother post-delivery reported when other rifamycins given with isoniazid in last weeks of pregnancy); limited risk data for breastfeeding	PIs: decreased concentrations of PIs; integrase inhibitors: increased concentration of raltegravir

\*Dose adjustment may be required in special situations † Route of Administration

## **Second line Anti TB-drugs**

TB medicines for use in treatment of MDR/RR-TB are categorized into Groups A, B and C. This new classification is based on drug class, and level of certainty in the evidence on effectiveness and safety (i.e., balance between benefit and risk of harm). At least 4-5 effective drugs should be used in DRTB treatment.

*Table 10 Second-line anti-tuberculosis drugs*

<b>Group and steps in constructing regimen</b>	<b>Medicine</b>	<b>Abbreviation</b>
<b>Group A</b>		
Include all three medicines	Levofloxacin OR	(Lfx)
	Moxifloxacin	(Mfx)
	Bedaquiline	(Bdq)
	Linezolid	(Lzd)
<b>Group B</b>		
Add one or both medicines	Clofazimine	(Cfz)
	Cycloserine	(Cs)
<b>Group C</b>		
Add to complete the regimen when medicines from Groups A and B cannot be used	Ethambutol	(E)
	Delamanid	(Dlm)
	Pyrazinamide	(Z)
	Imipenem-cilastatin OR	(Ipm-Cln)
	Meropenem	(Mpm)
	Amikacin	(Am)
	Ethionamide	(Eto)
	p-aminosalicylic acid	(PAS)

## **Other medicines used in treatment of drug resistant TB**

Pretomanid is a new drug which is tin the nitroimidazole group. It inhibits cell wall bio-synthesis hence has a bactericidal effect against mycobacterium. Dose: 200mg once a day.

### **Fixed-dose combinations**

Most often, TB drugs are administered in combination. When given within the same pill as a combination, they are referred to as fixed dose combination (FDC). The FDCs contain two or more drugs in a single tablet with strength (mg) of the drugs in each tablet known. Examples of FDC TB drugs used in the country include; 2-drug FDC [Rifampicin+ Isoniazid (RH)], 3-drug FDC [Rifampicin+ Isoniazid+ Pyrazinamide (RHZ)] and 4-drug FDC [Rifampicin+ Isoniazid+ Pyrazinamide+ Ethambutol (RHZE)]. There are scenarios where the drugs are not available as FDCs and thus administered as separate pills or drugs. FDC tablets have the following advantages:

- i.Prescription errors are minimised. Dosage recommendations are more accurate and adjustment of the dose according to patient weight is easier.
- ii.The patient has fewer tablets to swallow, which contributes to adherence.
- iii.If the treatment is not supervised, patients cannot be selective about which of the drugs to swallow.

### **TB treatment regimens**

Anti-TB drugs are administered in combinations called regimens. There are different regimens for DS-TB and DR-TB.

The regimens for DS-TB have the following characteristics:

- i. Contain at least one of the most effective anti-TB drugs (Rifampicin or Isoniazid) in both the initial and continuation phase of treatment
- ii. Must be written in abbreviation that clearly identifies the drugs in the initial and continuation phases of treatment
- iii. Defines a specific duration of treatment and frequency of giving the drugs
  - Duration in months is written in numbers in prefix for which the drugs that follow should be taken.
  - The forward slash (/) separates initial from continuation phase. For example, 2RHZE/4RH means an initial phase of two months consisting of daily Rifampicin, Isoniazid, Pyrazinamide and Ethambutol, followed by a 4-month continuation phase of Rifampicin and Isoniazid.

The regimens for DR-TB have the following characteristics:

- i. Contain at least one of the most effective anti-TB drugs
- ii. Must be written in abbreviation that clearly identifies the drugs
- iii. Defines a specific duration of treatment and frequency of giving the drugs
  - Duration in months is written in numbers in prefix for which the drugs that follow should be taken.
  - The slash (/) separates the initial from continuation phase. For example, 6BdQLfxCsCfzLzd/12LfxCsCfzLzd means 6 months of Bedaquiline Levofloxacin, Cycloserine, Clofazimine, and Linezolid and 12 months of Levofloxacin, Cycloserine, Clofazimine, and Linezolid

*Table 11 Recommended treatment regimen for drug sensitive TB based on disease classification*

Disease category and recommended treatment regimen		Comment
New patient	Previously treated patient	
2RHZE/4RH	2RHZE/4RH	Both new and previously treated TB patients should receive the same regimen provided rifampicin resistance has been excluded
2HPMZ/2HPM	2HPMZ/2HPM	<p>This is still a new regimen and may be used based on availability of the drugs. It should not be used for:</p> <ul style="list-style-type: none"> <li>- Patients weighing &lt;40kg,</li> <li>- People with certain forms of EPTB (TBM, disseminated TB, Osteoarticular TB, abdominal TB),</li> <li>- Persons living with HIV with CD4 count below 100 cells/mm<sup>3</sup>,</li> <li>- Children less than 12 years of age,</li> <li>- Pregnant, breastfeeding and postpartum women</li> </ul> <p>TB Meningitis, TB of the Bones &amp; joints, Spinal TB:</p>
2RHZE/10RH*		*Treatment duration may be extended depending patient's response to treatment; Steroids may be added as adjuvant therapy.

Table 12 Recommended treatment regimen for drug resistant TB based on disease classification

Regimen Type	Regimen composition	Eligibility criteria
The 6-month <b>BPaLM /BPaL</b>	6 Bedaquiline-Pretomanid-Linezolid-Moxifloxacin ( <b>BPaLM</b> ) or	Can be used in FQ resistance
	<b>BPaL</b> (without Moxifloxacin)	Preferred regimen for most patients >14 years except pregnant and breast-feeding mothers
The 6-month <b>BDLLfxC</b> regimen	<b>6BDLLfxC</b> (Bedaquiline-Delamanid-Linezolid-Levofloxacin-Clofazimine) or <b>BDLC</b> (without Levofloxacin) or <b>BDLLfx</b> (without Clofazimine)	Can be used in FQ resistance
		Preferred for children, adolescents, pregnant and breastfeeding women
The modified 9-month, all-oral regimens	<b>BLMZ, BLLfxCZ, BDLLfxZ and Bdq-Lzd-LfxCfz-Cs</b>	Cannot be used in FQ resistance
	BLMZ is preferred over BLLfxCZ, and BLLfxCZ is preferred over BDLLfxZ and BDLLfxZ is preferred over BLLfxCCs.	For patients not eligible for 6 months regimens
Longer regimens (> 18 months)	Designed using at least 4-5 effective drugs from the priority grouping of medicines recommended in current WHO guidelines	For patients not eligible for or have failed the shorter regimens
Rifampicin-susceptible Isoniazid resistant TB (Hr-TB).	<b>6 (RHZE-Lfx)</b>	Recommended irrespective of previous use of RHZE

The choice of treatment to administer to a TB patient is informed by a process, called treatment categorization where TB patients are grouped according to previous history of treatment i.e., new and previously treated TB patients:

**New patients** are TB patients with no prior history of TB treatment or had been treated for less than one month.

**Previously treated** patients have prior history of TB treatment, including: relapses, treatment failures and lost to follow up. The risk of drug resistance is higher loss among those lost to follow up and should therefore get a sputum test with an Xpert MTB/RIF/Ultra before re-initiation on any TB treatment.

Currently with the availability of rapid methods to identify key drug resistance such as the Xpert MTB/RIF/ultra-test, all patients presenting with a previous history of TB treatment are tested with Xpert MTB/RIF/ultra and if they do not have rifampicin resistance, they are treated with first line regimen. This development necessitated a new categorization of TB patients: Drug sensitive TB (DS TB) and rifampicin resistant TB (RR/MDR TB). DS TB patients are treated with first line TB drugs while RR/MDR TB patients are treated with second line TB drugs.

### Recommended Standard Regimens in Uganda

#### Susceptible TB

#### **First line: 2RHZE/4RH**

This is the current regimen for treatment of drug susceptible TB in Uganda and consists of 4 drugs and 2 treatment phases. The *initial phase* is the first two months of treatment. Using 4 drugs, results in rapid killing of the tubercle bacilli. Patients become non-infectious in about 2 weeks. Symptoms reduce, and most smear-positive cases become smear-negative within the first 2 months. *The continuation phase* lasts 2-4 months. Here, two drugs are used in combination, usually Rifampicin and Isoniazid (RH). For children and adolescents 3 months to 14 years of age with non-severe DS-TB disease, the continuation phase may last 2 months. For patients with TB meningitis and osteoarticular TB, the continuation phase is extended to 10 months.

### **Alternative regimen: 2HPMZ/2HPM**

This new regimen consists of two new drugs i.e., Rifapentine and Moxifloxacin. This regimen has been suggested as one way to shorten treatment of drug susceptible TB. It is a 4-month regimen (2HPMZ/2HPM) consisting of Isoniazid, Rifapentine, Moxifloxacin and Pyrazinamide. This new regimen is not available as a fixed dose combination (FDC) but not yet in use for adults. However, as supplies become available, the Ministry of health will guide on its roll out.

### **2RHZE/2RH**

This is a new regimen and is recommended for use in children (3 months to 14 years) with non-severe TB disease. This new regimen is already in use in the country. For more guidance, refer to the chapter of Child and Adolescent TB.

*Table 13 Recommended anti-TB drug doses for drug susceptible TB cases (> 15 years)*

Pre-treatment body weight(kg)	2-month initial phase	4-month continuation phase
	RHZE (150+75+400+275) mg	RH (150+75) mg
33-39	2 tablets	2 tablets
40-54	3 tablets	3 tablets
55-70	4 tablets	4 tablets
>70	5 tablets	5 tablets

*Note: If an adult is < 33kgs, determine the appropriate dose based on patient's weight*

### Drug resistant TB

These patients should be treated with a second line regimen which is used for treatment of RR/MDR-TB according to national RR/MDR-TB treatment guidelines. Current regimens are described in table 12 above.

### **Adjunctive therapy during TB treatment**

Non-anti-TB drugs are usually given to accompany anti-TB treatment. There are two such commonly used drugs, namely pyridoxine (Vitamin B6) and prednisolone.

i. **Pyridoxine:** This drug may be given to all TB patients once they start on treatment. Isoniazid interferes with the metabolism of pyridoxine in the body thus leading to its deficiency and hence peripheral neuropathy. Pyridoxine should thus be given in a dose of 25 mg daily for the entire duration the patient is on an Isoniazid containing regimen. In case of peripheral neuropathy, a high dose (up to max dose of 200mg) should be given until symptoms resolve, followed by maintenance (25mg) dose up to end of TB therapy. All DRTB patients using current regimen also require pyridoxine in doses of 50mgs and above (as required) for management of Linezolid related peripheral neuropathy.

ii. **Prednisolone:** This is a high potency anti-inflammatory drug, and is therefore useful in TB patients in whom complications of severe fibrosis are anticipated because of severe inflammation such as TB meningitis. Prednisolone is given in a dose of 1-2mg/kg body weight (not more than 60mg/day) as a single dose for four weeks, and then tapered off over two weeks.

Anti TB drugs are associated with some side effects., TB clients are encouraged to report any side effects to the health care worker immediately for appropriate support as shown in Table 14 below.

Table 14 Managing frequent side-effects of anti-TB drugs

Side-effects	Drug(s) likely to cause	Management
Low appetite, nausea, abdominal pain	Pyrazinamide, Rifampicin	Give drugs with small meals or just before going to bed
Joint pains	Pyrazinamide	Give an analgesic e.g., Ibuprofen or Paracetamol
Burning sensation in the feet	Isoniazid	Pyridoxine 25-100 mg daily (higher doses may be needed)
Orange/red urine	Rifampicin	Reassure the patient that it is not harmful
Skin rash	Any anti-TB drug	Stop anti-TB drugs, wait for patient to recover then reintroduce one drug at a time OR refer the patient. Take comprehensive history, assess the patient and consult a clinician for appropriate guidance.
Jaundice (other causes excluded)	Pyrazinamide, Rifampicin and Isoniazid	Take a comprehensive history, investigate the cause of jaundice; if it is due to anti TB medicines, stop the medicines till jaundice clears, then restart drugs
Mental confusion	Isoniazid, Rifampicin and Pyrazinamide	1. If jaundiced, suspect liver failure, treat as liver failure. 2 If no jaundice, suspect Isoniazid, increase dose of pyridoxine.
Visual impairment (other causes excluded)	Ethambutol	Stop Ethambutol. Refer to a higher level for further management.

Note: For any identified adverse event, the clinician should fill the adverse drug reaction form/report and notify NDA

## DS-TB TREATMENT MONITORING AMONG ADULT PATIENTS

Once a DS-TB TB patient is started on treatment, it is important to find out if the patient is getting better as a result of the treatment. This is called *treatment monitoring* and uses the following methods:

### Laboratory monitoring

Sputum microscopy must be used for monitoring all pulmonary TB patients. Sputum smears are performed as follows:

- i. For the 6 months regimen: At the end of the initial phase (2 months), at the beginning of 5 months and beginning of the 6th month of treatment.
- ii. For the 4 months regimen: At end of the initial phase (2 months), Week 12 (3 months) and end of treatment (end of 4 months).

This should be done for both smear-positive and smear-negative pulmonary TB patients. If the patient has a sputum smear that is positive at the end of the initial phase of treatment, consider the following as possible explanations:

- The treatment was poorly supervised
- The bacillary load was too high, e.g., in cavitary disease with slow clearance of the bacilli
- The patient could have RR/MDR-TB
- Could also be dead bacteria
- For patients registered as sputum smear-negative before the anti-TB treatment is started, clinical monitoring is recommended together with sputum monitoring. Sputum examination is important in these patients because:
  - An error could have occurred at the time of diagnosis
  - The patient may have drug-resistant TB

For patients on second line drugs, treatment monitoring should be done as for MDR TB patients. The GeneXpert should not be used for treatment monitoring. However, it can be used to exclude rifampicin resistance in patients who have positive sputum smears during treatment

### Messages for TB Patients

**1. TB is a disease caused by a germ (bacteria) that is very strong and difficult to kill by just one drug. The good news is, it can be treated and cured.**

**Because of this:**

- 2. The treatment uses a combination of more than one drug, and takes a long time (4-6 months). The treatment is divided into two parts. In the first part, lasting 2 months you will take more drugs than in the second part which lasts 2-4 months**
- 3. When you start and take TB medicines very well, the chances of transmitting TB to your dear ones reduces.**
- 4. Discuss with the health care worker, your preferred place where to get the TB medicines from.**

**During the 4- 6 months of your treatment:**

- 5. You will be requested to give sputum for examination at 2 months, 3 or 5 months and in the 4th or 6th month depending on the treatment regimen duration given. This is a continuous check to see how the drugs are working on the germs that caused the TB disease.**
- 6. Do not stop taking the medicines even if you feel well because TB will not be cured if you stop the drugs before the correct time has passed. You have to be discharged from treatment when you are confirmed cured by a health worker.**

**Should you feel the drugs are giving you problems**

- 7. Do not stop taking the drugs by yourself or on someone else's advice. Report your problem immediately to the health worker at the facility where you collect your drugs; you will be helped appropriately.**

**Remember**

This should be preceded by explanation about how TB spreads and risk of transmission to the family members, other close contacts etc

- 8. To bring your family members, and other close contacts to be checked for TB, particularly children under 5 years of age**
- 9. If you wish to change your residence before 4-6 months of treatment are completed, discuss with your health care provider who will link you to another health facility near your new residence**
- 10. When you cough, turn your face away from people. Cover your mouth with a handkerchief/mask or cough in the elbow**

**As a TB patient, it is important for you to know your HIV status. Take an HIV test now**

*The health worker should provide this information to the TB patients before starting treatment to facilitate adherence. Treatment education should be ongoing throughout the treatment period*

*Box 2 Monitoring treatment for adult DS-TB patients*

**Action points during treatment**

**At the end of the initial 2 months:**

If Sputum smear-negative, start the continuation phase  
If Sputum smear-positive, do GeneXpert or 10 color XDR assay. If GeneXpert shows RR or if INH monoresistance resistance is detected on 10 color, refer patient for drug resistance treatment and if Rif sensitive and no other resistance is noted, start the continuation phase. Explore and address adherence issues.

**At the end of 3 months (short regimen) or 5 months (long regimen)**

If Sputum smear-negative, continue with the continuation phase  
If Sputum smear-positive, diagnose treatment Failure  
Take sputum for GeneXpert and or 10 color XDR assay to rule out RR and any other resistance.  
If RR, refer for DR treatment.  
If MTB detected but not RR, re-start the first line regimen but explore and address adherence issues.  
A sample for full DST should be taken off and sent to NTRL immediately.

**At the end of 4 months (short regimen) or 6 months (long regimen)**

If Sputum smear-negative, complete treatment and declare cured or treatment completed  
If Sputum smear-positive, diagnose treatment failure  
Take sputum for GeneXpert and or 10 color XDR assay to rule out RR.  
If RR, refer for DR treatment.  
If MTB detected but not RR, restart first line regimen but explore and address adherence issues. Take off a sample for full DST and send it to NTRL

**Clinical monitoring** –is useful for all patients but is particularly useful for children and extra-pulmonary TB cases. Treatment monitoring is carried out through clinical observation/assessment. A patient's weight gain and reduction in symptoms are useful indicators.

**Radiological monitoring** –is a method that should not be used as the sole monitoring tool. In cases where radiological monitoring is used, sputum and clinical monitoring should accompany the radiological monitoring.

### **Monitoring and recording adverse effects**

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 are clinically monitored during treatment so that adverse effects are promptly detected and appropriately managed. Routine laboratory monitoring is not necessary. Health personnel can monitor adverse drug effects by teaching 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 medicines for reviews.

Adverse reactions to drugs should be recorded on the TB Treatment Card under "comments" and treatment register under the remarks section. The attending clinician should record the adverse event in the adverse drug reaction form/portal and notify the National Drug Authority (NDA).

*The pharmacovigilance information monitoring system (PVIMS) is a national platform where all drug reactions should be reported for every adverse event detected and managed.*

## Defining Treatment Outcome

A conclusion should be made regarding treatment outcome for every TB patient who has started on anti-TB treatment within the same year (reporting period). The treatment outcomes for DS-TB and DR-TB have recently been changed as shown in box 3 below.

*Box 3 Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB)*

### Treatment outcome definitions

- a) **Treatment failed:** A patient whose treatment regimen needed to be terminated or permanently changed to a new regimen or treatment strategy
- b) **Cure:** A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who completed treatment as recommended by the national policy, with evidence of bacteriological response and no evidence of failure.
- c) **Treatment completed:** A patient who completed treatment as recommended by the national policy, whose outcome does not meet the definition for cure or treatment failure
- d) **Died:** A patient who dies before starting treatment or during the course of treatment
- e) **Lost to follow-up:** A patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more
- f) **Not Evaluated:** A patient whom no treatment outcome was assigned
- g) **Treatment success:** The sum of cured and treatment completed.

*Table 15 Managing TB treatment interruption*

Duration of interruption	Action	Sputum result	Decision
0-2 months	Trace the patient	NA	Re-initiate on treatment (same regimen)
	Identify and address the cause, if possible		
	Adherence counselling		
2 or more consecutive months, i.e., loss to follow-up	Trace the patient	GeneXpert negative	Clinical decision on individual basis whether to restart
	Identify and address the cause	GeneXpert positive	If Rifampicin resistance detected
	Do GeneXpert and/or 10 colour XDR assay,		Refer to MDRTB treatment. Obtain sputum for full DST before treatment initiation at DRTB unit
	No treatment while waiting for results		If Rifampicin resistance not detected and no other resistance has been detected from the 10 colour XDR assay
			Restart first line TB treatment regimen

## TUBERCULOSIS CARE AND SUPPORT

The End TB strategy emphasizes a person-centred approach to TB treatment and management, promoting adherence to prescribed medications through tailored support interventions. Over time, adherence strategies have expanded beyond DOT services to include SMS reminders, phone calls, digital adherence technologies, patient education, psychosocial support, counselling, appointment reminders, and directly observed treatment. Adherence involves taking the correct drug at the right time, dose, and frequency to achieve optimal outcomes.

Patients receiving treatment support—whether community-, home-, or facility-based—demonstrate higher treatment success, adherence, and sputum conversion rates, with lower mortality, loss to follow-up, and drug resistance compared to those on self-administered treatment (SAT). Community- or home-based support, provided near patients' homes or workplaces, outperforms facility-based support in treatment success, completion, and cure rates.

Combining multiple adherence interventions improves treatment outcomes and reduces mortality and loss to follow-up more effectively than single interventions or SAT alone.

### **Care and support interventions for all people with TB**

1. Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment
2. A package of treatment adherence interventions may be offered to patients on TB treatment in conjunction with the selection of a suitable treatment administration option
3. One or more of the treatment adherence interventions (tracers, social support, psychological support, staff education) may be offered to patients on TB treatment or to health-care providers. These interventions are complementary and not mutually exclusive. The treatment adherence interventions are listed in *Table 16* below.
4. Treatment support options may be offered to patients on TB treatment. The options include:
  - Community- or home-based treatment support recommended over health facility-based treatment support or unsupported treatment.
  - Treatment support by trained lay providers or health-care workers is recommended over treatment support by family members or unsupported treatment.
  - Digital adherence support may replace in-person treatment support when the digital adherence technology is available and it can be appropriately organized and operated by health-care providers and patients.

*Table 16 Treatment adherence interventions*

<b>Treatment adherence intervention</b>	<b>Description</b>
<b>Patient education</b>	Health education and counselling on facts about TB
<b>Staff education</b>	CPD, chart or visual reminder, IEC materials and desk job aid for decision-making and reminder
<b>Social support</b>	Food or financial support such as meals, food baskets, food supplements, food vouchers, transport subsidies, living allowance, housing incentives or financial bonus. This support addresses indirect costs incurred by patients or their attendants in accessing health services and, possibly, tries to mitigate the consequences of income loss related to the disease.
<b>Psychological support</b>	Counselling sessions or peer-group support
<b>Tracer</b>	Communication with the patient, including home visit or via mobile telephone communication such as SMS or telephone (voice) call
<b>Digital adherence technologies (DAT)</b>	Video directly observed treatment (VDOT) – use of smart mobile phone to record videos whenever taking the medicines and sending the video to the health worker Pill Box The pillbox can give audio reminders or send an SMS to remind the patient to take medications, and send a signal to a health worker whenever a patient opens the box to take the medicine.

Tracers have been found to improve treatment success, treatment adherence and 2-month sputum conversion, and lower rates of mortality, loss to follow-up and drug resistance acquisition. The tracers could include home visits or mobile telephone communication (SMS or telephone call).

Social support including material support for patients has potential to protect patients and their households against catastrophic costs associated with TB. Some of these interventions include: giving meals for treatment support, monthly food vouchers, food baskets, food supplements and vitamins. Patients who receive this support have higher rates of treatment success, completion and sputum conversion compared with patients who do not receive the support.

In regard to treatment refill and support, community-based or home-based treatment refill and support has more advantages than health facility-based treatment support. Treatment refill and support is better provided at home or in the community by trained lay providers or health-care workers.

### **Engaging Private Providers in CB-DOTS Implementation**

Private providers play a big role in diagnosing and treating TB. Efforts have been made by the NTLP to engage some of the private providers to ensure appropriate delivery of TB services through a coordinated framework. The different categories of private providers who can play a role in managing presumptive and diagnosed TB patients include:

- i.Private for profit (PFP) health providers
- ii.Private, not-for-profit hospitals and health centres including the faith-based organisations/bureaus
- iii.Individual private physicians, nurses, midwives, clinical officers, etc.
- iv.Pharmacies and drug shops
- v.Practitioners of traditional medical systems

The NTLP can engage the private providers in several ways depending on the capacity and operational level of the private provider. The public-private mix (PPM) DOTS strategy shall include but not be limited to:

- i.NTLP Training health workers in large hospitals and clinics, on the identification of patients with presumptive TB patients and diagnosis of TB. The health workers in these large hospitals and clinics should also be trained to carry out recording and reporting using the NTLP monitoring and evaluation tools. The trained private facility can be supported to get accredited and acquire a DHIS2 reporting screen otherwise it can serve TB patients under a nearby public health facility to which accountability of both patients, and medicines is made periodically.
- ii.The support to private providers by NTLP & the District Health Office to:
  - Conduct training for health workers of the smaller private provider units so that they can recognize and refer patients with presumptive TB to diagnostic facilities and keep a record of such referrals.
  - Conduct regular training and targeted supervision to update private providers on current TB management recommendations.
  - Provide private provider facilities with support supervisory visits to ensure that the private providers carry out their work according to NTLP recommendations.
  - Support the provision of necessary logistics to aid the diagnosis and treatment. The logistics could include sputum mugs, laboratory reagents/supplies and TB drugs.
  - Monitor private providers to ensure they do not charge TB patients for the anti-TB drugs provided.

## Facility based DOT

Patients can have their anti-TB treatment observed daily by the health worker at the health facility at least during the intensive phase of treatment. Patients that live near the health facility or those admitted can benefit from facility DOT where possible.

## Tuberculosis/Leprosy Mortality surveillance

The Registration of persons Act - in 2015, mandates registration of death events. Reliable and timely information on cause-specific mortality data is a critical part of identifying emerging health problems and a fundamental component of evidence-based health policy development, implementation, and evaluation. The WHO Score Assessment conducted in 2016 and 2019 indicated limited capacity on mortality surveillance among the Member States. Patients suffering or have suffered TB or leprosy may die not as a consequence resulting from the disease. Medical certifiers fulfil an important final step in completing a patient's care by providing cause of death for the death certificate. A properly completed cause-of-death section provides an aetiological explanation of the order, type, and association of events resulting in death. It is important to ensure these records are completed as accurately as possible.

Figure 14 Required flow of events for medical certificate of cause of death

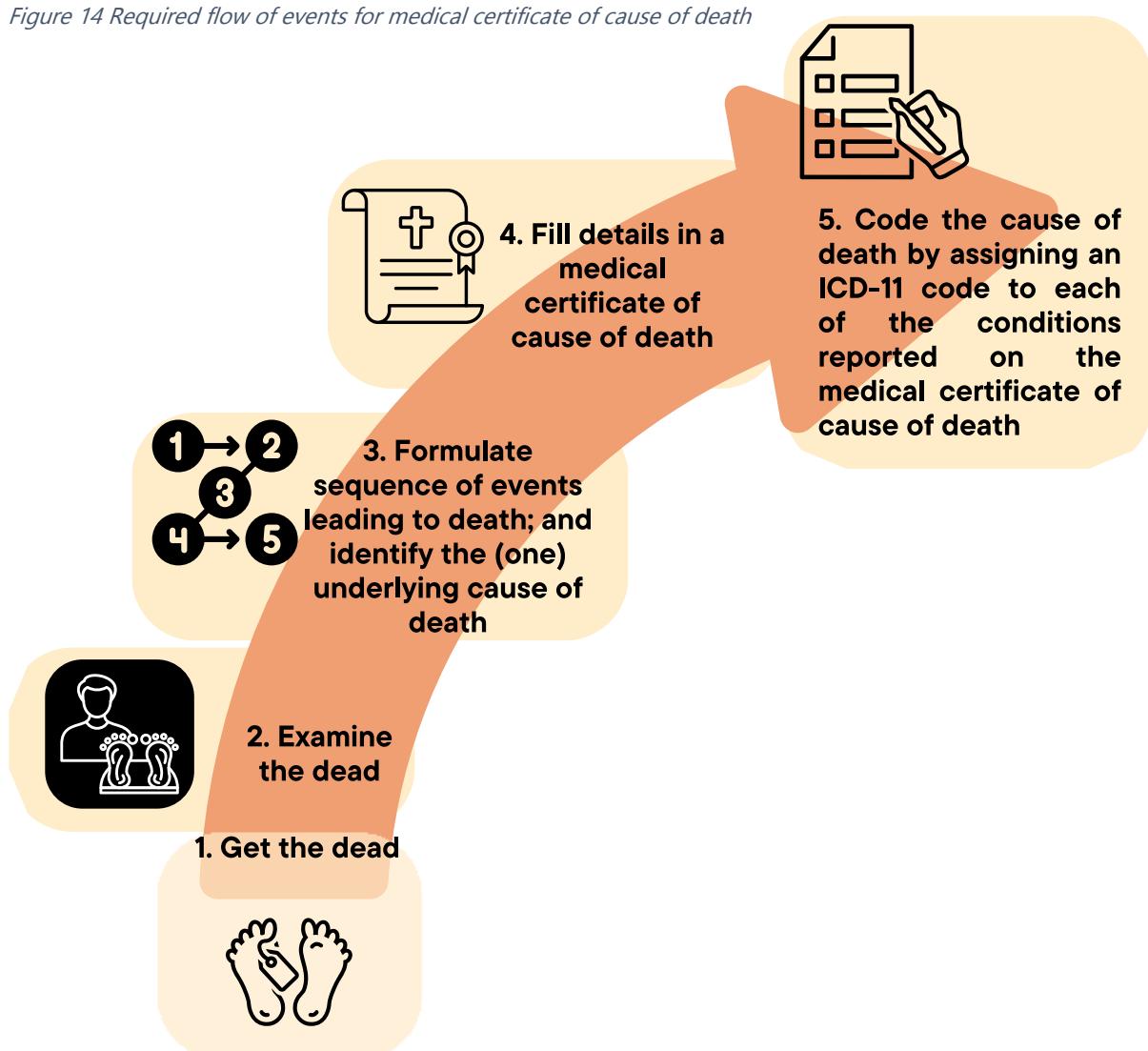


Table 17 Cause of Death Instructions – Completing a Certificate of Death

<b>Part I: Chain of Events Leading Directly to Death</b>
<b>Immediate Cause:</b> Enter the final disease, injury, or complication directly causing death on Line (a)
<b>Underlying Cause:</b> Enter the condition initiating the chain of events on the lowest line used.
Use only one cause per line. Line (a) MUST ALWAYS be completed; additional lines can be added as needed.
If the condition on Line (a) resulted from another, list the underlying condition on subsequent lines (b, c, etc.).
Include the time interval between the onset of each condition and death.
<b>Avoid Listing Terminal Events</b> (e.g., cardiac arrest).
For neoplasms, specify: 1 Primary site (or unknown), 2. Benign/malignant, 3. Cell type (or unknown), 4. Grade, and 5. Affected part or lobe of the organ. (Example: Primary well-differentiated squamous cell carcinoma, lung, left upper lobe.)
<b>Part II: Contributing Conditions</b>
List other significant diseases, conditions, or injuries that contributed to death but were not part of the chain of events in Part I.
<b>Note:</b> Cause-of-death details should reflect your best medical opinion and adhere to ICD-11 coding.
<b>Manner of death</b>
Classify based on the type and circumstances of the condition(s): <ul style="list-style-type: none"> <li>• <b>Natural:</b> Solely due to disease or aging.</li> <li>• <b>Unnatural:</b> Caused by injury or poisoning (external causes).</li> <li>• <b>Undetermined:</b> If the manner cannot be established, describe as undetermined.</li> </ul> Refer to Annex HMIS100 for further details.
<b>Terminology:</b>
<ul style="list-style-type: none"> <li>• <b>Immediate Cause of Death:</b> The final condition causing death, listed on line (a) in Part I.</li> <li>• <b>Intermediate Causes:</b> Conditions linking the immediate cause to the underlying cause.</li> <li>• <b>Underlying Cause of Death:</b> The condition initiating the sequence leading to death, reported on the lowest line in Part I.</li> <li>• <b>Interval Between Onset and Death:</b> The time between the onset of each condition and death, indicating how long the patient had the condition, not how long it was diagnosed.</li> </ul> This information should reflect your best medical opinion.

### Important points

- Definition of cause of death does not include symptoms, Signs and modes of dying such as cardiorespiratory arrest and respiratory failure.
- Always use consecutive lines starting at 1(a), never leave blank lines within the sequence
- If there is only one cause of death, it is entered at 1(a)
- Each condition below 1(a) is a cause of the condition above it, i.e. it is an antecedent cause
- The initiating cause in the sequence is the Underlying Cause
- The entry must be legible. Use black ink.
- Do not use abbreviations.
- Enter only one disease condition or event per line.
- As much detail as possible should be recorded so that it can be used to assign complete and specific codes from the ICD
- The medical certificate of cause of death is to be approved/ signed by a qualified/licensed medical doctor
- The medical certificate of cause of death is sent to the registering authority (NIRA) through DHIS2,
- The medical cause of death should be maintained by the facility and NIRA for confidentiality of the deceased information on the cause of death.

## Case study

A 58-year-old man presented at a clinic with a long history of haemoptysis and weight loss. The diagnosis was advanced pulmonary tuberculosis, reactivation type with cavitation, perhaps of eight years duration. The patient also suffered from generalised arteriosclerosis, probably of long duration. Directly after the admission, the patient had an acute and massive pulmonary haemorrhage and died about 10 hours later. The patient's death certificate is shown below;

*Table 18 Case study on TB mortality*

<b>Frame A: Medical data: Part 1and 2</b>				
<b>1 Report disease or condition directly leading to death on line (a)</b>			Cause of death	Time interval from onset to death
	a	Pulmonary haemorrhage	10 hours	
Report chain of events in due to order (if applicable)	b	Due to: Advanced pulmonary tuberculosis	8 years	
	c	Due to:		
State the underlying cause on the lowest used line	d	Due to:		
<b>2 Other significant conditions contributing to death (time intervals can be included in brackets after the condition)</b>	Generalised arteriosclerosis (unknown)			

Note: All deaths of any TB patient should be notified using the HMIS100, audited at the TB unit to ascertain cause of death, and a medical certificate of cause of death documented in the DHIS2 (Annex).

## **TB and Leprosy Differentiated Service delivery (DSD) models**

TB and Leprosy DSD is a people-centred approach which prioritizes people-centred care and health system efficiency. It refers to various ways of providing screening, diagnosis, treatment and preventive services that are tailored to the needs and preferences of people who have TB or leprosy or those at risk of TB or leprosy infection with the aim of maintaining good clinical outcomes and improving efficiency in service delivery.

### **Rationale for TB and Leprosy DSD**

TB and Leprosy patients have diverse needs and hence require tailored TB/Leprosy care and treatment services. TB and Leprosy DSD, at both facility and community levels, focus on:

- i. Targeted, people-centred TB and Leprosy screening
- ii. Supporting TB and Leprosy diagnosis by promoting both facility and community sample collection
- iii. Modifying client flow, schedules and location of TB and leprosy Care, Treatment and Prevention services for improved access, coverage and quality of care
- iv. SBCC to increase both client and provider literacy to empower individuals to make desirable health decisions and support adoption/utilization of TB/Leprosy differentiated services

### **The building blocks of TB/Leprosy DSD.**

TB/Leprosy DSD is premised on four questions:

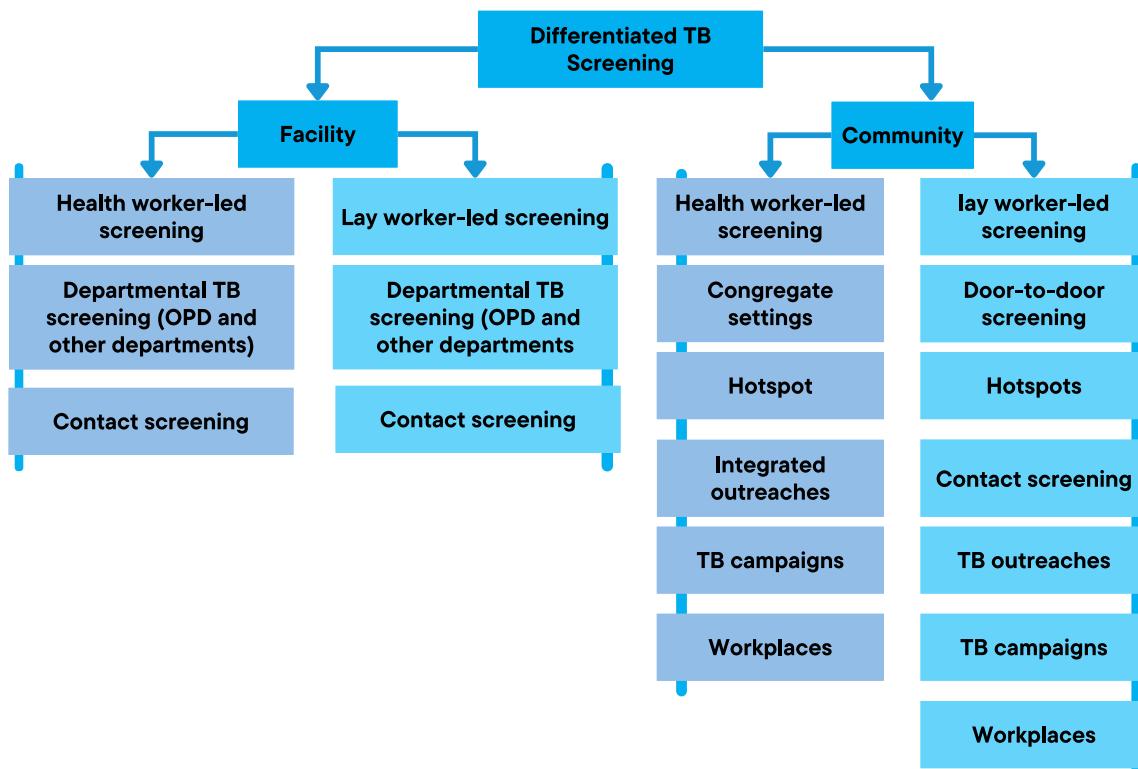
- **What?** (Services needed by the clients e.g., Screening, testing, prevention, treatment and Contact Tracing)
- **When?** (Weekly, Monthly, Two months, three months and Four months)
- **Where?** (At Home, community and health facility)
- **Who?** (Physician, Clinician, Community health worker, Peer and Family member)

### **DIFFERENTIATED TB AND LEPROSY SCREENING, TESTING/DIAGNOSIS.**

Differentiated TB/leprosy screening are highly targeted client-centred service delivery models to actively locate TB/leprosy cases; tailored to meet the needs of all sub-populations of patients/clients at both facility and community levels.

Recommended models and approaches for Differentiated TB/Leprosy Screening, Testing/Diagnosis are shown in the schema below

Figure 15 Schema for Differentiated TB screening, testing/diagnosis



### Differentiated TB and Leprosy Care and Treatment

This refers to a strategic mix of approaches to address the specific requirements of a subgroup of TB and leprosy patients.

It includes approaches aimed at modifications of client flow, schedules and location of TB /leprosy Care and Treatment services for improved access, coverage, quality of care and treatment outcomes.

### TB/Leprosy patient categorization for differentiated service delivery

Patient categorization should be informed by a comprehensive assessment of factors, including;

- Patient's clinical condition,
- Disease severity, sputum conversion status,
- TB drug sensitivity,
- Presence of comorbidities
- Any observed adverse drug reactions.

Table 19 below shows a structured framework to guide patient categorization based on the above parameters.

Table 19 DSD categorisation of patients

Drug sensitive TB		Drug-resistant TB	
Well patient	Unwell patient	Well patient	Unwell patient
Has no danger signs or signs of severe illness.	Has danger signs and/or signs of severe illness.	Has no danger signs or signs of severe illness.	Pre/XDR TB
If HIV/Co-infected, has no other AHD illness	If HIV/Co-infected, has other AHD illness e.g. CCM, severe pneumonia, severe bacterial infections, or another stage 3 or 4 illness.	If HIV/Co-infected, has no other AHD illness	Has danger signs and/or signs of severe illness.
Controlled Comorbidities if any	Has un-controlled comorbidities	Controlled comorbidities if any	If HIV/Co-infected, has other AHD illness e.g CCM, another stage 3 or 4 illness.
Has a negative Sputum smear at the end of month 2 and 5	Has a positive Sputum at end of month 2 and/or month 5	Has culture converted	Has un-controlled comorbidities
	Has drug ADR/AEs		Has drug ADR/AEs
			Has not culture converted or has culture reverted
Leprosy			
Well Leprosy Patient		Unwell Leprosy Patient	
Has no disability		Has leprosy reaction or any other leprosy complications	
Controlled comorbidities, if any		Has disability grade 1 or 2	
Has no leprosy reaction or other leprosy complication		Uncontrolled comorbidities	

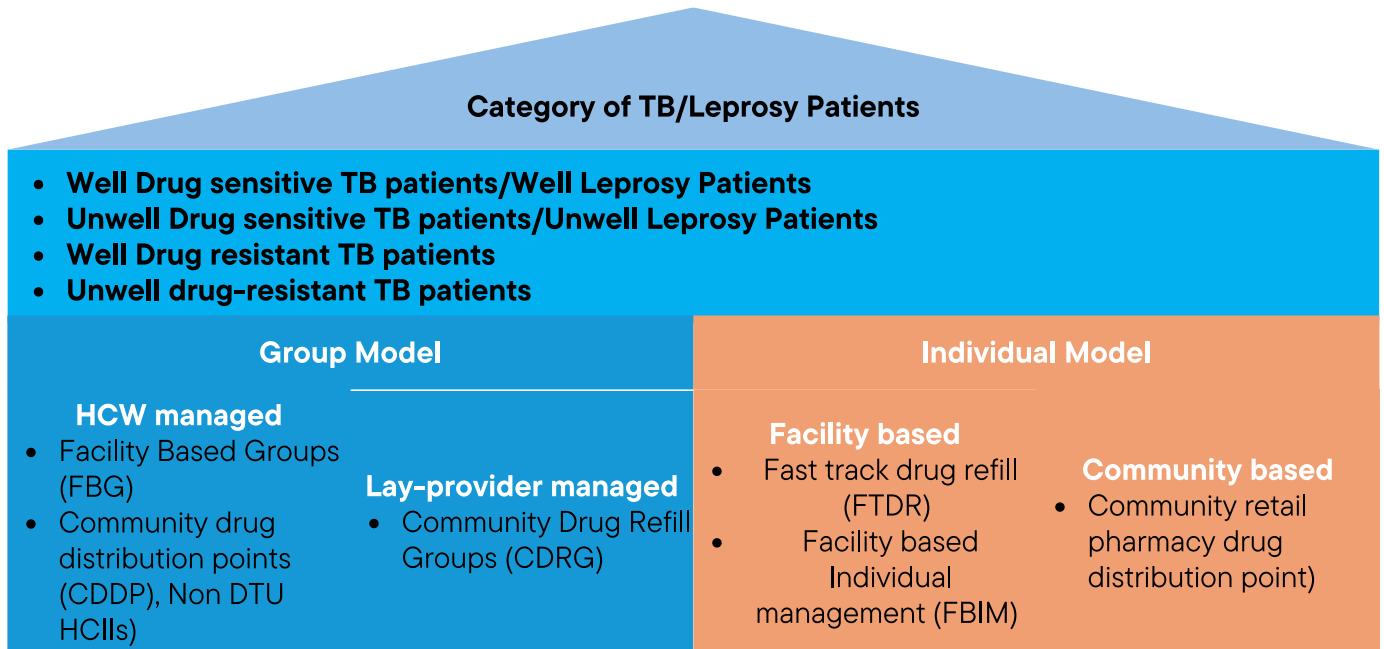
### Eligibility criteria for the models

The 5As (Assess, Advise, Assist, Agree, Arrange) will be used to assess for model suitability at each physical or virtual encounter with the client as shown in Table 20 below.

Table 20 Model eligibility criteria

Disease	Patient category	Group models managed by Health worker	Group models managed by Lay provider	Individual models based at facility	Individual models based in the community
Drug sensitive TB and leprosy patients	Well patient	✓	✓	✓	✓
	Unwell patient	✓		✓	✓
Drug resistant TB	Well patient	✓		✓	✓
	Unwell patient			✓	

Figure 16 differentiated care and treatment service delivery models and their respective TB/Leprosy patient categories



### Multi Month TB Medicine dispensing

Offer longer dispensing intervals, if the medicine stock level permits. Shorter clinical review visits should not hinder the dispensation of long duration medicine refills i.e., de-link the medicine refill frequency from clinical assessment frequency.

During the intensive phase, up to 2 months medicines refills can be offered depending on the patient's condition and circumstances. Offer up to 3 months refill during the TB treatment continuation phase and for Leprosy patients.

DR TB patients under community DOTs including Digital adherence technologies (DAT) can be offered one month refill

### DIFFERENTIATED TB/LEPROSY PREVENTION SERVICES

Differentiation of TB and Leprosy prevention services entail reorientation of TB prevention services to overcome the unique access barriers faced by populations at risk of TB disease, those likely to spread TB disease, or those with sequel of TB disease.

#### Differentiated TB Preventive Treatment.

TPT will be initiated at the health facility or in the community by a qualified health worker as shown in Figure 16 above.

## **Digital adherence technologies**

With the expansion of mobile phone and cellular access including in high-TB-burden countries in Africa, digital adherence technologies (DATs) may facilitate alternative approaches for improving adherence. These technologies range from cell phone short messaging service (SMS) texts, to digital pillboxes, to ingestible sensors.

DATs may help to remind patients to take their medications, facilitate digital observation of pill-taking, compile dosing histories and triage patients based on their level of adherence, which can facilitate provision of individualized care by TB programs to patients with varied levels of risk.

In 2017, video directly observed therapy (VDOT) was endorsed as an alternative to DOT for monitoring treatment where possible. VDOT enables the patient to use a smartphone to record videos of their daily pill intake without face-to-face interactions with the health providers. VDOT can overcome the limitations of in-person DOT at the patient and health system levels.

VDOT studies have shown that the distance barrier is mostly eliminated, patients have greater autonomy to choose when and where to take their medications, the costs of travel are minimized, and providers can support a higher number of patients, thus increasing the health system efficiency.

## TUBERCULOSIS PREVENTIVE TREATMENT

Currently a quarter of people worldwide are infected with TB bacilli. The vast majority have no signs or symptoms of TB disease and are not infectious, although they are at risk of developing active TB disease and becoming infectious.

Studies have shown that in recent decades, on average, 5–10% of those infected with TB will develop active TB disease over the course of their lives. The risk for active TB disease after infection depends on several factors, the most important being immunological status.

Preventive treatment of TB is the use of anti-TB drug(s) to prevent the development of active TB disease in an individual who has latent TB infection (LTBI). Prevention of active TB disease by TB preventive treatment has been suggested as a critical component of the WHO End TB Strategy and efforts to eliminate TB. Probably TB elimination will occur once there is wide use of LTBI treatment. LTBI therapy has been shown to reduce the risk of developing active TB by over 60% in several studies. The efficacy varies according to the regimen used and the duration.

**To prevent the progression of LTBI to active TB, TB Preventive Treatment (TPT) is recommended for the following categories of individuals:**

- HIV positive persons irrespective of TST results and CD4 cell count.
- Under five-year child contacts of persons with pulmonary bacteriologically confirmed TB.
- Exclusion of active TB using the available screening algorithms is highly recommended.

## Diagnosis of latent TB

Prior to initiation of TB preventive treatment, it is important to confirm LTBI and rule out TB disease. LTBI is confirmed through several methods. The commonest methods are:

- i. Tuberculin skin test (TST) also called Mantoux
- ii. TB antigen-based skin test (TBST)
- iii. Interferon-gamma release assay (IGRA)

There is no gold standard test to diagnose LTBI and currently available tests – TST, TBST and IGRA are indirect and require a competent immune response to identify people infected with TB. A positive test result by either method is not by itself a reliable indicator of the risk of progression to active disease.

TST is positive when the induration of TST has a diameter of equal or more than 5 mm in an HIV-positive person and 10mm or more mm in an HIV- negative person. Each of the tests has its advantages and disadvantages. Both TST and TBST require a return visit by the patient to read the result. TBST and IGRA test outcomes are not affected by presence of BCG vaccination or non-tuberculosis mycobacteria.

**Confirmation of LTBI using IGRA, TBST or TST and reliable exclusion of active TB with chest radiography would be desirable before starting TB preventive treatment. In situations where these tests are not available, TPT should not be withheld from eligible people if active disease has been excluded on clinical grounds alone.**

## **Target populations for TB preventive treatment**

The highest risk for reactivation of LTBI to active TB disease occurs in the populations below, and they are therefore the key target populations for TB preventive therapy

- i. Adults and adolescents living with HIV
- ii. Infants and children living with HIV
- iii. Household contacts of pulmonary TB patients
- iv. Persons living in congregate settings e.g., Prisoners,
- v. Persons with immunosuppression e.g., patients receiving dialysis, patients preparing for organ or haematological transplant, patients initiating anti-TNF, patients with silicosis.

## **Tests for tuberculosis infection**

Tests for latent TB infection: The tuberculin skin test includes tests like Mantoux test (skin prick test), Tuberculosis antigen-based skin tests (TBST) and interferon-gamma release assays (IGRA). These tests cannot distinguish TB infection from TB disease and cannot predict who will progress to TB disease. These tests should therefore not be used in screening of TB disease.

Tuberculosis antigen-based skin tests are a more recent form of latent TB infection test. Examples include CY-TB, C-TST and Diaskin test. The manufacturer recommends administration using the Mantoux method – intradermally. The manufacturers recommend reading of the reaction at the injection site 48–72 hours after injection. The transverse and longitudinal diameter of the induration should be measured, and the average diameter of the induration should both be recorded (calculated as the sum of the transverse and longitudinal diameters, divided by two). The presence of blistering, necrosis (skin breakdown) or lymphadenitis is recorded and interpreted as a strong positive reaction.

*Table 21 Criteria for a positive TBST*

Diaskin	Negative: absence of infiltration (induration) or hyperaemia or the presence of a "prick response" up to 2 mm
	Ambiguous: the presence of hyperaemia without infiltrate (induration)
	Positive: the presence of infiltrate (induration or papule) of any size
	Poorly expressed response infiltration size up to 5 mm
	Moderately expressed response infiltration size 5–9 mm
	Pronounced response: infiltration size 10–14 mm
	Hyperergic response: infiltration size 15 mm or more, with vesiculo-necrotic alterations or lymphangitis or lymphadenitis, regardless of the infiltration size
CY-TB	Induration $\geq$ 5 mm
C-TST	Average diameter (sum of transverse and longitudinal diameters, divided by 2) of redness or induration $\geq$ 5 mm
	Blister, necrosis (skin breakdown) or lymphadenitis are interpreted as strong positive reactions

## **Tuberculosis preventive treatment options**

TB preventive treatment for an infection with strains presumed to be drug-susceptible can be broadly categorized into two types: monotherapy with isoniazid for at least 6 months (or isoniazid preventive therapy, IPT) and treatment with regimens containing a rifamycin (rifampicin or rifapentine). IPT has been the most widely used form of TB preventive treatment but the shorter duration of rifamycin regimens presents a clear advantage.

The following options are recommended for the treatment of LTBI regardless of HIV status:

- 6 months of daily isoniazid (6H) or
- 3-month regimen of weekly rifapentine plus isoniazid (3HP)
- month regimen of daily rifapentine plus isoniazid (1HP)
- 3-month regimen of daily isoniazid plus rifampicin

Until recently, 6H has been the only available regimen for TPT among eligible HIV positive persons and contacts of pulmonary bacteriologically confirmed TB patients aged <5 years. NTLP has updated the TB preventive treatment guidelines to include the new treatment regimens which are shorter with less pill burden to ensure improved uptake and adherence. Health workers are encouraged to consult the TPT guidelines when considering initiating TPT. It is important that before TPT is initiated, active TB is excluded. This is done to avoid monotherapy for active TB, because TB should always be treated with combination therapy.

The choice of TPT option to use is determined by many factors such as: age, risk of toxicity or interaction, co-morbidity, drug susceptibility of the strain of the most likely source case, availability and the individual's preferences.

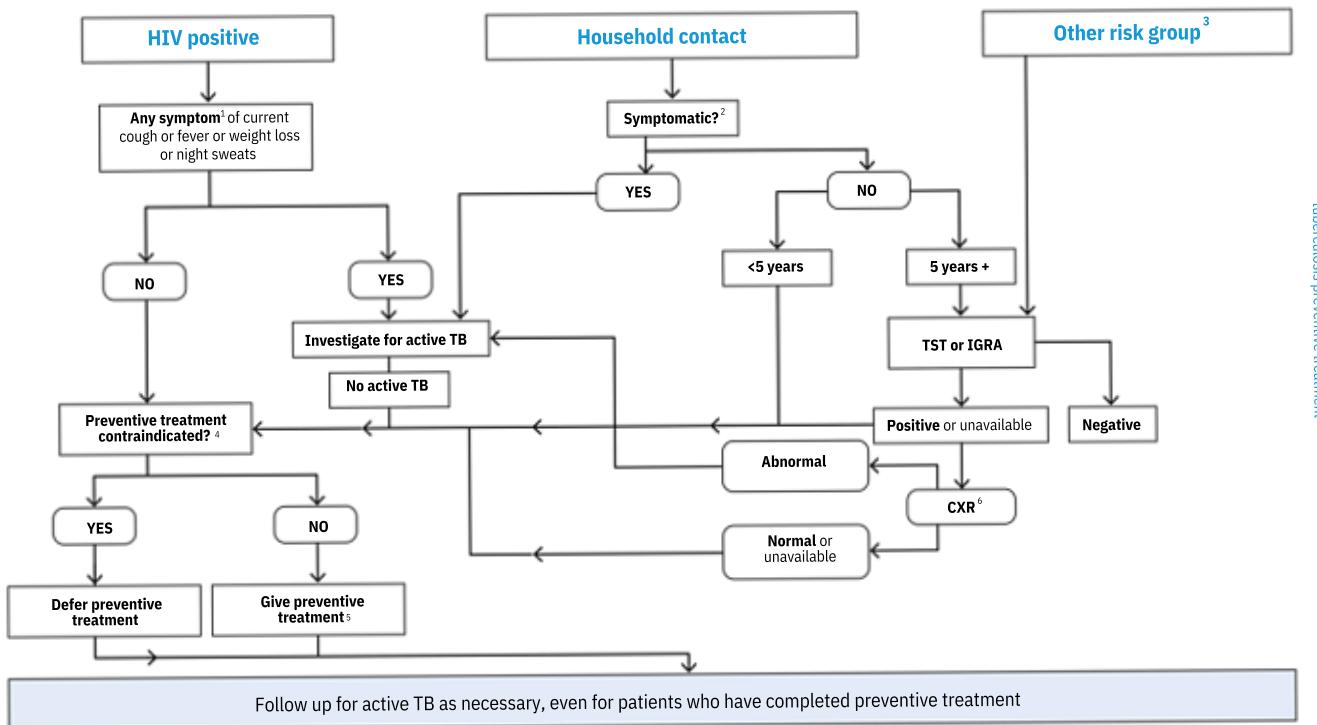
**Uganda in 2021 adopted the use of shorter 1-month and 3-month TPT regimens. Where these supplies are available, they should be used.**

**As there is limited data on the performance and pharmacology of rifapentine in children < 2 years. 3HP regimen is only recommended for use in children aged 2 years or more**

The following should be noted:

- i. Adults and adolescents living with HIV should be screened for TB according to a clinical algorithm. Those who do not report any of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered preventive treatment, regardless of their ART status
- ii. Adults and adolescents living with HIV who are screened for TB according to a clinical algorithm and who report any of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases and offered preventive treatment if active TB is excluded
- iii. Chest radiography may be offered to people living with HIV on ART and preventive treatment be given to those with no abnormal radiographic findings
- iv. All infants and children living with HIV who have poor weight gain, fever or current cough or who have a history of contact with a person with TB should be evaluated for TB and other diseases that cause such symptoms. If TB disease is excluded after an appropriate clinical evaluation, these should be offered TB preventive treatment
- v. The absence of any symptoms of TB and the absence of abnormal chest radiographic findings may be used to rule out active TB disease among HIV-negative household contacts aged  $\geq$  5 years and other risk groups before preventive treatment
- vi. Tuberculin Skin Test (TST), TBST or IGRA are not a requirement for initiating TPT among PLHIV or < 5-year-old TB contacts, and should not be a barrier to TPT among 5+ year old contacts and other high-risk groups.
- vii. Providing TPT does not increase the risk of developing drug resistant TB. Therefore, concerns regarding the development of resistance should not be a barrier to providing TPT.

Figure 17 Algorithm for LTBI testing and TB preventive treatment in individuals at risk



- If <10 years, any one of current cough or fever or history of contact with TB or reported weight loss or confirmed weight loss >5% since last visit or growth curve flattening or weight for age <-2 Z-scores. Asymptomatic infants <1 year with HIV are only treated for LTBI if they are household contacts of TB. TST or IGRA may identify PLHIV who will benefit most from preventive treatment. Chest radiography (CXR) may be used in PLHIV on ART, before starting LTBI treatment.
- Any one of cough or fever or night sweats or haemoptysis or weight loss or chest pain or shortness of breath or fatigue. In children <5 years, they should also be free of anorexia, failure to thrive, not eating well, decreased activity or playfulness to be considered asymptomatic.
- Including silicosis, dialysis, anti-TNF agent treatment, preparation for transplantation or other risks in national guidelines.
- Including acute or chronic hepatitis; peripheral neuropathy (if isoniazid is used); regular and heavy alcohol consumption. Pregnancy or a previous history of TB are not contraindications.
- Regimens chosen based on considerations of age, strain (drug susceptible or otherwise), risk of toxicity, availability and preferences.
- CXR may have been carried out earlier on as part of intensified case finding.

Table 22 Recommended regimens and dosages of medicines for TB preventive treatment

Regimen	Dose by weight band
6 months of daily isoniazid monotherapy (6H, 9H)	Age 10 years & older: 5 mg/kg/day Age <10 years: 10 mg/kg/day (range, 7–15 mg)
Four months of daily rifampicin (4R)	Age 10 years & older: 10 mg/kg/day Age <10 years: 15 mg/kg/day (range, 10–20 mg)
Three months of daily rifampicin plus isoniazid (3HR)	Isoniazid: Age 10 years & older: 5 mg/kg/day Age <10 years: 10 mg/kg/day (range, 7–15 mg) Rifampicin: Age 10 years & older: 10 mg/kg/day Age <10 years: 15 mg/kg/day (range, 10–20 mg)
Three months of weekly rifapentine and isoniazid (3HP) equivalent to 12 doses	Adult: 900mg INH/ 900mg RPT Children: Weight-banded paediatric dosing for 10 kg–40 kg * 300mg formulation can be used to reduce pill burden
One month of rifapentine plus isoniazid daily (28 doses) (1HP)	Age ≥13 years (regardless of weight band) Isoniazid, 300 mg/day Rifapentine, 600 mg/day

**In Uganda, the recommended TPT options are:**

- 3-month regimen of weekly rifapentine plus isoniazid (3HP)
- 1-month regimen of daily rifapentine Isoniazid (1HP)

## **TPT in different groups of individuals**

The following section highlights the TPT guidelines for different categories of individuals.

### **TPT in children**

Providing treatment for TB infection to prevent TB disease is a critical aspect of TB control. Several regimens are currently available with their efficacy ranging from 60% to 90%.

TPT is recommended for the following categories:

A. Infants, children and adolescents with HIV:

- Adults and adolescents living with HIV who are unlikely to have TB disease should receive TPT as part of a comprehensive package of HIV care.
- Infants aged under 12 months living with HIV who are in contact with a person with TB and who are unlikely to have TB disease on an appropriate clinical evaluation or according to Uganda national guidelines should receive TPT
- Children aged 12 months and over living with HIV who are considered unlikely to have TB disease on an appropriate clinical evaluation or according to Uganda national guidelines should be offered TPT as part of a comprehensive package of HIV prevention regardless of contact with TB

B. Household/close contacts (regardless of HIV)

- Children aged under 5 years who are household/close contacts of people with bacteriologically confirmed PTB and who are found not to have TB disease on an appropriate clinical evaluation or according to Uganda national guidelines should be given TPT
- Children aged 5 years and over and adolescents who are household/close contacts of people with bacteriologically confirmed PTB who are found not to have TB disease by an appropriate clinical evaluation or according to Uganda national guidelines may be given TPT
- In selected high-risk household/close contacts of people with MDR-TB, TPT may be considered based on individualized risk assessment and a sound clinical justification

**It is important to exclude TB disease before initiating TPT**

### **TPT options in children**

When 6H was the main regimen used for TB preventive treatment, the term "isoniazid preventive therapy" (IPT) was often used to refer to TB preventive treatment in general. Since many alternative regimens to IPT are now recommended, the term "TB preventive treatment" is preferred.

*Table 23 TPT Recommended regimens in Uganda*

<b>Regimen</b>	<b>Recommended groups</b>
3HP	<ul style="list-style-type: none"> <li>• Children living with HIV aged ≥2 years</li> <li>• Adolescents living with HIV</li> <li>• HIV negative contacts ≥5 years</li> </ul>
6H	<ul style="list-style-type: none"> <li>• Children &lt;2 years</li> <li>• PLHIV on protease inhibitors.</li> </ul>
3HR	<ul style="list-style-type: none"> <li>• HIV negative contacts &lt;5 years</li> </ul>

**3HR is a preferred TPT option among HIV-negative children since child-friendly dispersible FDCs are widely available and already used for TB treatment, while awaiting data on dosages across all age groups and child-friendly formulations for rifapentine-based regimens. For children living with HIV, 6H remains the preferred option until further data are available**

### **BCG Vaccination:**

Another way to prevent TB in children beyond the TPT is immunisation with BCG. The BCG vaccine is a live attenuated vaccine administered to all new born babies according to the national Expanded Program of Immunisation (EPI) guidelines. The vaccine provides up to 90% protection against severe forms of TB, including TB meningitis and miliary TB, if given during the neonatal period. Although neonatal vaccination also provides protection against PTB in children, it mainly prevents progression to disseminated forms of TB. BCG vaccinated children who have contact with people with infectious TB have 19% less TB infection than their unvaccinated counterparts.

BCG should not be administered to children with confirmed HIV infection because they are at increased risk of developing disseminated BCG disease.

### **Household contacts of pulmonary TB**

For these individuals, the following are the recommendations:

1. Children aged < 5 years who are household contacts of people with bacteriologically confirmed pulmonary TB and who are found not to have active TB on an appropriate clinical evaluation or according to national guidelines should be given TB preventive treatment
2. Children aged ≥ 5 years, adolescents and adults who are household contacts of people with bacteriologically confirmed pulmonary TB who are found not to have active TB by an appropriate clinical evaluation or according to national guidelines may be given TB preventive treatment

### **Contacts of MDR-TB patients**

Uganda has not started giving TPT to contacts of MDR TB patients but will be considered among selected high-risk household contacts of patients with MDR-TB patients, and will be based on individualized risk assessment and a sound clinical justification. For now, strict clinical observation and close monitoring for the development of active TB disease for at least two years and application of TB infection control measures at home as well as instituting effective therapy for the index case should be done.

## **Pregnancy**

TPT in pregnancy is not entirely safe, thus advisable that TPT is initiated after pregnancy. The pregnant mother should be evaluated for TB throughout pregnancy.

## **Other people at risk**

- People who are initiating anti-TNF treatment, or receiving dialysis, or preparing for an organ or haematological transplant, or who have silicosis should be systematically tested and treated for LTBI
- Systematic LTBI testing and treatment may be considered for prisoners, health workers, immigrants from countries with a high TB burden, homeless people and people who use drugs
- Systematic LTBI testing and treatment is not recommended for people with diabetes, people who engage in the harmful use of alcohol, tobacco smokers and underweight people unless they also belong to other risk groups included in the above recommendations (i.e., pregnant, HIV positive)

## **Drug interactions**

Rifampicin induces certain cytochrome P-450 enzymes and may therefore interfere with medicines that depend on this metabolic pathway, hence accelerating their elimination. Regimens containing rifampicin should be prescribed with caution to PLHIV who are on ART because of potential drug–drug interactions.

These regimens should not be administered to people receiving protease inhibitors or nevirapine, including HIV-exposed infants on preventive treatment.

No dose adjustment is required when rifampicin is co-administered with efavirenz (EFV). The dose of dolutegravir (DTG) however needs to be increased to 50 mg twice daily when given together with rifampicin.

## **Monitoring TPT for toxicity and management of adverse events**

Medicines for TB preventive treatment are generally safe, but adverse reactions may occur. Isoniazid can cause asymptomatic elevation of liver enzymes, peripheral neuropathy, and hepatotoxicity, while rifampicin and rifapentine may cause skin reactions, hypersensitivity, gastrointestinal issues, and hepatotoxicity. Though rare and usually minor, preventing drug-induced hepatotoxicity is crucial.

Symptoms of hepatotoxicity to watch for include anorexia, nausea, vomiting, abdominal discomfort, fatigue, dark urine, pale stools, or jaundice. Baseline and periodic liver function tests (AST, ALT, bilirubin) are strongly recommended for individuals with liver disease, alcohol use, chronic liver issues, HIV, pregnancy, postpartum status (within three months), or those over 35 years old.

Patients on TPT should have monthly check-ups, where healthcare providers explain the treatment and its importance. Patients must report symptoms like anorexia, nausea, vomiting, abdominal discomfort, fatigue, dark urine, pale stools, jaundice, confusion, or drowsiness immediately. If healthcare is unavailable, patients should stop treatment at the onset of such symptoms.

## **Standards for facilitating TPT adherence and completion**

Adherence to treatment is crucial for both individual health and program success. Therefore, everyone eligible for TPT should receive counselling and health education, including follow-up sessions for treatment monitoring. Health education supports adherence by guiding individuals on reporting adverse events, understanding risks and benefits, and staying motivated to complete treatment.

Education should cover TB transmission, prevention, treatment options for infection and disease, and when to contact healthcare workers about adverse effects or treatment interruptions.

Health education sessions must clearly distinguish between TB infection and disease, emphasizing that TPT significantly reduces the risk of progression. Patients should be informed about potential TPT side effects to enable timely reporting.

These sessions can also promote healthy behaviours, such as good nutrition and smoking cessation, discuss integrating treatment into daily routines to improve adherence, and address risk factors like HIV or diabetes. Families and household members, especially caregivers of children, should also receive education, as they play a key role in administering medication.

*Table 24 Components of health education and counselling session*

<b>Key points for health education</b>	(i) Structured and comprehensive educational programmes are an integral and essential component of the management of TPT (ii) Educational programmes should be age-specific, gender and culturally sensitive, delivered in the local language and extended to mothers and families/households (iii) Education should be delivered by professionals who are competent in the relevant subject areas and trained to deliver educational sessions (iv) Educational materials and technological support used to deliver them needs to be evaluated in the setting-specific context
<b>Recommended topics for counselling</b>	(i) Basic principles of TB: epidemiology, clinical aspects and transmission routes (ii) Difference between TB disease and TB infection, role of TPT in reducing progression (iii) Importance of TPT (and treatment adherence/retention in care) to reduce the risk of developing TB disease in the presence of TBI (iv) Simple concepts of infection control and safety procedures (v) Advantages/importance of smoking cessation and risk of comorbidities (e.g., HIV co-infection and DM) in household/families (vi) Ensuring adequate nutrition and refraining from alcohol consumption (vii) Importance of adhering to medical prescriptions for the management of comorbidities and vaccinations (viii) Recognition of drug adverse effects and the need to report to healthcare providers (ix) Information on how to contact the healthcare provider if needed (x) Discussing with the individual what potential barriers are for TPT completion and how these can be addressed/overcome (adherence plan)

If an individual on TPT develops active TB, TPT must immediately be stopped and instead, a fully-fledged appropriate TB regimen is provided based on the patient's TB category.

**Note: TPT is treatment of latent TB infection**

## DRUG-RESISTANT TUBERCULOSIS

### Burden of Drug Resistant-Tuberculosis

In 2019, WHO estimated that 1% of new cases and 12% of previously treated cases were MDR/RR-TB cases. According to the Uganda Drug resistance survey done in 2010, the prevalence of MDR-TB among newly diagnosed TB (Primary MDR-TB) patients was 1.4 %. Among previously treated patients, isoniazid resistance occurred in 21.1%, rifampicin resistance was detected in 12.1%. A second drug resistance survey (DRS2 2023) to shed more light on the current burden of drug resistant TB in Uganda is being conducted and in its final stages.

### Definition of Drug Resistant TB (DR-TB)

Drug resistance is said to occur when TB organisms continue to grow in the presence of one or more anti-TB drugs.

### Forms of drug-resistant tuberculosis

- **Mono-resistance:** resistance to one first line anti-tuberculosis drug
- **Poly-resistance:** resistance to more than one first line anti-tuberculosis drug, other than both Isoniazid and Rifampicin
- **Isoniazid-resistant TB (Hr-TB)** is caused by *Mycobacterium tuberculosis* strains resistant to isoniazid and susceptible to rifampicin
- **Rifampicin-resistant TB (RR-TB)** is caused by *M. tuberculosis* strains that are resistant to rifampicin. RR-TB strains may be susceptible to isoniazid or resistant to it (i.e., MDR-TB), or resistant to other first-line or second-line TB medicines.
- **Multidrug-resistant TB (MDR-TB)** is caused by *M. tuberculosis* strains that are resistant to at least both isoniazid and rifampicin.
- **Pre-XDR TB** is TB caused by *Mycobacterium tuberculosis* strains that fulfil the definition of multidrug resistant and rifampicin resistant TB (MDR/RR-TB) and which are also resistant to any fluoroquinolone.
- **Extensively drug-resistant TB (XDR-TB)** is TB caused by *Mycobacterium tuberculosis* (*M. tuberculosis*) strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group A drug

### Risk factors for DR-TB

Although several factors can contribute to the development of drug-resistant TB, inadequate anti-TB treatment is probably the most important. Inadequate anti-TB treatment leads to mutation in drug-susceptibility bacilli making them drug resistant. Overgrowth of initially drug-resistant bacilli also occurs when inadequate anti-TB treatment is used. Below are situations of inadequate anti-TB treatment:

- Inadequate drug regimen
- Inadequate duration of treatment
- Drugs not taken regularly by the patient
- Use of poor-quality drugs

Factors causing inadequate anti-TB treatment can be grouped into health provider factors, drug factors and patient factors.

*Table 25 Factors contributing to an inadequate anti-TB regimen*

Categories	Factors
Health care providers: Inadequate regimens	Inadequate DOT Non-compliance with guidelines or absence of guidelines Limited capacity of health care workers Poor monitoring of treatment Wrong dose or treatment regimen Inadequate patient education Weak patient support mechanisms Suboptimal management of adverse events
System Challenges/ issues	Low quality medicines Unavailability of all or certain drugs (stock-outs or delivery disruptions) Poor storage conditions Poor regulation of medicines Poorly organised or under-funded programs
Patient factors	Poor adherence Poverty Lack of transportation Adverse effects Social barriers Malabsorption Diabetes mellitus Alcohol and substance abuse Other comorbidities

## **Diagnosis of DR-TB**

### **Risk groups for drug resistance**

Drug resistance TB can be suspected under the following circumstances (risk groups):

- Contact with known drug-resistant tuberculosis
- Relapses
- Treatment after failures
- Return after loss to follow up
- History of frequent interruption of drug treatment
- HIV-positive patient presumed to have TB
- Patients who remain sputum smear-positive at month 2 or 3 months of first-line anti-TB treatment
- Health care workers
- Patients from prisons or other congregate settings
- Chronic cases (still sputum smear-positive after completing a supervised retreatment regimen)

## **Laboratory testing for DR-TB**

Drug susceptibility testing (DST) is crucial for diagnosing DR-TB and guiding the use of WHO-recommended treatment regimens. Reliable, quality-assured DST is emphasized in current guidelines. Rapid molecular tests, such as GeneXpert MTB/RIF, Truenat, GeneXpert MTB/XDR, and Line Probe Assays (LPA), detect MDR/RR-TB and other resistance types by identifying genetic markers, enabling timely and precise treatment decisions.

GeneXpert MTB/RIF Ultra and Truenat will be used for initial rifampicin resistance testing among TB patients. GeneXpert MTB/XDR will serve as a point-of-care test at DR-TB treatment centres to detect resistance to isoniazid, fluoroquinolones, ethionamide, and second-line injectables, guiding regimen selection before treatment initiation. LPA, centralized at the NTRL, will support additional resistance testing when XDR cartridges are unavailable or machines are down. Definitive drug resistance diagnosis relies on phenotypic DST, with specimens taken for culture and DST to guide MDR-TB regimens and monitor treatment outcomes.

## **Treatment of Drug-Resistant Tuberculosis in adults**

Initiation of DR-TB treatment and any modification of such treatment should be done by the DR-TB Expert Review Panels in DR-TB treatment initiation centres. Treatment of DR-TB depends on the resistance pattern; whether it is mono- or poly- resistant or whether it is multidrug - or extensively resistant tuberculosis. Treatment regimens should be constructed for these patients based on DST patterns. The most effective treatment regimens shall be reviewed by specialists and approved by Expert Review Panels in the DR-TB treatment initiation centres for every DRTB patient.

Patients with a diagnosis of MDR-TB or XDR-TB should have treatment started as soon as possible.

## **Drugs for treatment of DR-TB in adults**

*Table 26 Drugs for treatment of DR TB*

<b>Group and steps</b>	<b>Medicine</b>	<b>Abbreviation</b>
<b>Group A</b> Include all three medicines	Levofloxacin OR Moxifloxacin Bedaquiline Linezolid	(Lfx) (Mfx) (Bdq) (Lzd)
<b>Group B</b> Add one or both medicines	Clofazimine Cycloserine	(Cfz) (Cs)
<b>Group C</b> Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol Delamanid Pyrazinamide Imipenem-cilastatin OR Meropenem Amikacin Ethionamide p-aminosalicylic acid	(E) (Dlm) (Z) (Ipm-Cln) (Mpm) (Am) (Eto) (PAS)

It is important that before treatment for MDR TB is initiated, a laboratory confirmation is done. However, in some instances this is not possible and empirical treatment is done. Empirical treatment refers to the initiation of treatment before laboratory confirmation of the drug-resistance pattern. Empirical treatment can be either standardised or individualised.

- i. Standardized treatment is one in which the composition and duration of treatment are to a large extent fixed. The treatment regimens are designed based on DST data from representative patient populations, and all patients in a defined group or category receive the same regimen. This is usually done in the absence of individualised DST and may be changed once individual results are available. Standard regimen should be used if susceptibility to fluoroquinolones is documented (or almost certain)
- ii. Individualised treatment is one in which a regimen is designed based on the patient's past history of TB treatment and individual DST results.

#### **Duration of DR-TB treatment and treatment regimens**

DR TB may require longer treatment periods than susceptible TB in some cases. Previously, most of the DRTB treatment regimen included injectable drugs in addition to oral medicines. However, newer and repurposed drugs have been developed which have enabled TB programs to shift to much shorter all-oral MDRTB treatment regimen that can range from 6 months to 18 months of treatment. The treatment duration depends on regimen used, drug resistant type and response to treatment. This is also associated with less side effects and together with shortened treatment periods is anticipated to improve adherence to treatment and ultimately improve patient outcomes. Based on the drug resistance identified and duration, the following are the current treatment regimens available.

- Regimen for isoniazid-resistant TB: 6 (H)REZ-Lfx (6-month treatment regimen composed of rifampicin, ethambutol, pyrazinamide, levofloxacin. As most often REZ is not available as a standalone, FDCs that have Isoniazid (H) can be used together with Lfx (6 (H)REZ-Lfx).
- Shorter regimen for MDR/RR-TB in patients with MDR/RR-TB where fluoroquinolone susceptibility is presumed or documented. with quinolone resistance: 6 Bdq-Pa-Lzd-Mfx (6-month treatment regimen composed of Bedaquiline, Pretomanid, linezolid and Moxifloxacin – BpaLM regimen). It is possible to omit moxifloxacin and continue with the BPaL regimen for MDR/RR-TB patients with confirmed fluoroquinolone resistance

Whereas in drug sensitive TB where treatment is in two phases (intensive and continuation phase), in DR TB, some options allow treatment in a single phase e.g., the regimen for Isoniazid resistance allows for a single-phase treatment of 6 months. A shorter regimen for MDR/RR TB using Bedaquilline, Pretomanid and Linezolid (BPaL regimen) can also be administered in a single phase for fluoroquinolone resistant TB

## **Drug resistant TB treatment regimens**

The following treatment regimens are currently available.

### **i. Regimen for rifampicin- susceptible and isoniazid- resistant TB (Hr-TB):**

This regimen is used once isoniazid resistance has been confirmed and rifampicin resistance excluded. In these patients, treatment with rifampicin, ethambutol, pyrazinamide and levofloxacin is recommended for a duration of 6 months.

The recommended regimen in this group of patients is **Hr-TB regimen: 6(H)REZ-Lfx**

The medications for rifampicin susceptible and isoniazid resistant TB are administered daily for 6 months. In instances where fixed-dose combination formulations are used, isoniazid is included but is not a must for the regimen.

**It is not advisable to give a regimen for Hr-TB unless isoniazid resistance is confirmed or highly suspected (e.g., confirmed TB patient who is the close contact of a documented Hr-TB case).**

**The regimen recommended for treatment of Hr-TB does not have an intensive and a continuation phase**

The clinical monitoring of patients on Hr-TB treatment follows similar principles to those that apply to other first-line TB regimens. Bacteriological monitoring of sputum generally follows the same schedule as DS TB, with direct microscopy at months 2, 5 and 6. It is desirable, however, to perform a culture together with smear microscopy (at least in the last month of treatment) to check for any emergent resistance, especially to rifampicin.

### **ii. The short 6 months BPALM/BPAI regimen.**

This regimen includes two Bedaquiline-containing options and is the preferred choice for most patients with MDR/RR-TB. It is a standardized, 6-month, all-oral treatment composed of Bedaquiline, Pretomanid, Linezolid, and Moxifloxacin. This regimen is specifically used for patients with MDR/RR-TB who have documented or presumed susceptibility to fluoroquinolones.

#### **Eligibility for BPALM/BPAI regimen**

Pulmonary TB or all forms of extrapulmonary TB, except TB involving the CNS, osteoarticular TB and disseminated (miliary) TB;

1. Patient is aged 14 years or older;
2. No known allergy to any of the BPALM component drugs;
3. No evidence of resistance to Bedaquiline, Linezolid, Delamanid or Pretomanid,
4. Patient has not been previously exposed to any of the component drugs for 4 weeks or longer; with no confirmed resistance.
5. All people regardless of HIV status
6. No XDR-TB according to the 2021 WHO definitions; and
7. Premenopausal women willing to use effective contraception.

All medicines in the regimen are to be used throughout treatment duration. Ideally, missing doses of all three or four drugs in the regimen should be avoided. When the regimen is BPaL from the start or is changed to BPaL, BPaL can be extended to a total of 9 months (39 weeks) continuing from the start of the therapy with BPaLM/BPaL.

Extension of the BPaL regimen to a total of 9 months can occur in cases where:

1. There is a delayed culture conversion between months 4 and 6,
2. There is a proven fluoroquinolone resistance
3. There are persons with extensive disease (i.e., bilateral, cavitary disease with significant fibrosis, or scarring/cavities in 3 or more lung zones).
4. Any interruption with BPaLM/BPaL of longer than 7 days should be made up for by extending the treatment duration (for the number of missed doses).
5. Any treatment interruption with BPaLM/BPaL up to 1 month nonconsecutively or 14 days of consecutively can be added to the overall treatment.

**Note:** Extension of BPaL to 9 months should be done with caution in patients with missed Linezolid dosages for two weeks – switching to an Individualised longer regimen may be considered instead of a BPaL extension. 26 weeks of BPaLM or 39 weeks of BPaL of prescribed doses should be completed within an overall period of 7 or 10 months, respectively. 9months BPaL regimen and long Individualised regimen are recommended for management of Pre-XDR TB, however the National Panel will decide basing on a case scenario.

### **6 months BDLLfxC (Bedaquiline, delamanid, linezolid, levofloxacin, and clofazimine)**

This regimen is also used for the eligible MDR/RR TB patients with or without fluoquinolone resistance who may include children, pregnant and breast-feeding women. The New modified 9- months treatment regimens include:

1. BLMZ (Bedaquiline, Linezolid, Moxifloxacin, Pyrazinamide)
2. BLLfxCZ (Bedaquiline, Linezolid, Levofloxacin, Clofazimine, Pyrazinamide)
3. BDLLfxZ (Bedaquiline, Delamanid, Linezolid, Levofloxacin, Pyrazinamide)

These regimens are preferred over the currently used 18-20months longer regimen. It will be used for those eligible and do not benefit from the BPaLM regimen

#### **iii. Longer Individualised regimens for MDR/RR-TB**

These regimens have a duration of at least 18 months, individually designed based on the hierarchical grouping of second-line TB medicines, the drugs resistance profile and patients' medical history.

In ideal conditions, only a small proportion of MDR/RR-TB patients should opt or be considered for longer regimens, because this indication is mainly for those who cannot benefit from either BPaLM/BpaL or the 9-month all-oral (STR) regimen.

Patients with MDR/RR-TB who are not eligible for or had no favourable treatment outcome using the above 6-month or 9-month regimens, have strains with extensive drug resistance eg., XDR or have intolerance to key components in the above-mentioned regimens.

However, the longer regimen is preferably given to those MDR/RR-TB patients who are not eligible for shorter all-oral regimens, including those with quinolone resistance. They are used when; there is intolerance to key medicines used in shorter regimens, severe TB disease, XDR TB and in TB involving the CNS, osteomyelitis and arthritis

All patients being considered for a longer MDR-TB treatment regimen should have a laboratory- confirmed diagnosis of MDR/RR-TB before embarking on a regimen using second-line medicines.

### **Stepwise Approach in Designing MDR-TB Individualised regimen**

- Step 1: Choose all drugs in Group A unless there is intolerance or resistance
- Step2: Choose all drugs in Group B unless there is intolerance or resistance
- Step 3: Choose all drugs in Group C if unable to compose a regimen using Group A and B drugs

### **Treatment of MDR-TB and RR-TB in children and adolescents**

It is estimated that between 25,000 and 32,000 children and young adolescents aged under 15 years develop MDR-TB disease annually. Contact investigation and screening of child and adolescent contacts of infectious MDR/RR-TB source cases are essential for the rapid diagnosis of children with MDR/RR-TB disease and for prompt initiation of treatment.

Children with clinically diagnosed or bacteriologically confirmed MDR/RR-TB should be treated with a WHO-recommended treatment regimen.

A clinical diagnosis of MDR/RR-TB can be made based on a clinical diagnosis of TB and either exposure to a known case of MDR/RR-TB or presence of other risk factors for MDR/RR-TB (e.g. child treated previously for TB or exposed to a source case who died from TB or failed TB treatment). Up to 83% of the time, children are very likely to have TB with the same resistance pattern as their most likely source case.

### **Multidrug-resistant and rifampicin- resistant TB treatment regimens**

The risks and benefits of each medicine should be considered carefully while designing a regimen. Generally, most of the available second line drugs can be used in children. However, Pretomanid which is the most recent molecule introduced in the 6 months shorter (BPALM) regimen (WHO,2022) cannot be used in children due to lack of available drug dosing evidence in children and pregnant mothers.

#### **i. Regimen for rifampicin- susceptible and isoniazid- resistant TB (Hr-TB) Hr-TB regimen: 6REZ-Lfx**

This regimen is used once isoniazid resistance has been confirmed and rifampicin resistance excluded. In these patients, treatment with rifampicin, ethambutol, pyrazinamide and levofloxacin is recommended for a duration of 6 months.

As there is no FDC for this regimen, the available FDCs can be used to constitute the regimen. For example, paediatric formulations of RHZ + E + Lfx for children < 25 kg and adult formulations of RHZE + Lfx for children and adolescents > 25kg could be used.

#### **ii. Regimens for MDR/RR-TB for children and adolescents**

The most recently recommended 6 month all oral MDR TB treatment regimen for use in children under 15 years of age is BDLLFx (Bedaquiline, Delamanid, levofloxacin, Linezolid and Clofazimine). This regimen can be tailored to patient drug sensitivity profile to fluoroquinolones where DST for fluoroquinolone (FQ) is available (BDLLFx for FQ sensitive patients and BDLLC for FQ resistant patients (WHO, rapid communication 2024).

For children not eligible for this 6months regimen, the modified 9 months all oral regimen including BLMZ, BLLfxCZ, and BDLLfxz may be used to manage the children and adolescents with non-extensive RR/MDR TB disease without resistance to fluoroquinolones, or previous exposure to second line drugs. In general, the treatment principles for MDR/RR-TB in children follow those recommended for adolescents and adults. Access to rapid DST (10 colour XDR) for ruling out fluoroquinolone resistance is required before starting a patient on one of these regimens.

The 9-month, all-oral, Bedaquiline-containing regimens are preferred over the longer (>18 months) regimens in adults and children with MDR/RR-TB, without previous exposure to second-line treatment (including Bedaquiline), without fluoroquinolone resistance and with no extensive pulmonary TB disease or severe forms of extrapulmonary TB. In these regimens, 2 months of linezolid (600 mg) can be used as an alternative to 4 months of ethionamide.

Patients with extensive forms of DR-TB (e.g., XDR-TB) or those who are not eligible for or have failed shorter treatment regimens will benefit from individualised longer ( $\geq 18$  months) regimens designed using the priority grouping of medicines recommended in current WHO guidelines.

Decisions on appropriate regimens should be made according to clinical judgement and patient preference, considering DST results, treatment history, risk of adverse events, and severity and site of the disease.

### **iii. Longer regimens for MDR/RR-TB**

This consists of 18-month treatment regimen composed of Bedaquiline for the first 6 months and levofloxacin or moxifloxacin, linezolid, clofazimine for 18 months (18 Bdq (6 m)-Lfx/Mfx-Lzd-Cfz) and should be used in children not eligible for the standardized all-oral Bedaquiline-containing regimen.

Children who are not eligible for the all-oral 6 and or 9 months Bedaquiline-containing regimens should be treated with the longer individualised treatment regimens. In general, the treatment principles for MDR/RR-TB in children follow those recommended for adolescents and adults.

#### **Monitoring MDR TB treatment response**

#### **Monitoring treatment response and outcome assignment**

To monitor the treatment response in patients on MDR-TB regimens, it is strongly recommended that sputum culture be repeated at monthly intervals, in addition to sputum smear microscopy.

Monthly culture increases the detection of patients with a true positive bacteriological result when compared with sputum smear microscopy alone. In addition, it reduces the proportion of patients with a false negative result. Regular microscopy and culture of sputum or other specimens remain important to ensure that treatment failure is detected early and ensures appropriate action is instituted early. Using smear microscopy or culture to assess conversion of

bacteriological status is an important means of assessing response, and most patients are expected to have converted to a sputum negative status within the first few months of starting treatment.

In children, it is difficult to make a diagnosis of DR TB (due to difficulty in obtaining bacteriological sputum samples). However, the SOS (single one step stool analysis) can now be used to confirm the rifampicin resistance in children where sputum sample cannot be obtained. Therefore, in children with a bacteriologically confirmed diagnosis, all reasonable efforts should be taken to demonstrate bacteriological conversion.

### **Active drug safety and management (aDSM) of adverse events**

This is the active and systematic clinical and laboratory assessment during treatment to detect drug toxicity and adverse events. It includes routine screening, identification, documentation, management and reporting of adverse events. In DR TB, this is done during the monthly clinic reviews.

All detected adverse events should be documented in the client form, managed well and reported through the electronic based pharmacovigilance management information system (PIVIMS) which has been rolled out at all the DRTB management sites. The use of PIVIMS improves visibility of adverse events to the clinicians and program teams which can be used to improve quality of care for the patient.

### **Adjuncts to MDR-TB treatment**

#### **Surgery in treatment of MDR/XDR-TB**

Surgery has been employed in the treatment of TB. The updated WHO consolidated guidelines include a conditional recommendation for elective partial lung resection (lobectomy or wedge resection) as an adjunct to chemotherapy of MDR/RR-TB and XDR/TB patients. Such would help to reduce the amount of lung tissue with intractable pathology and to reduce the bacterial load.

#### **Use of corticosteroids**

Corticosteroids are used to support the treatment of serious and severe consequences of TB, such as military TB, respiratory insufficiency, CNS involvement and pericarditis.

In patients with tuberculous meningitis, an initial adjuvant corticosteroid therapy with dexamethasone or prednisolone tapered over 6–8 weeks should be used.

In patients with tuberculous pericarditis, an initial adjuvant corticosteroid therapy may be used.

Corticosteroids suppress immunity and could weaken the body's ability to mount a response against TB. They should thus only be used if clearly indicated and if the patient is on an adequate effective regimen as use in inadequate regimen could accelerate the patient's deterioration.

## **Models of care for people with drug-resistant TB**

For these patients, the recommendations are as follows:

1. Early ambulatory model of care is recommended for patients with MDR-TB over prolonged hospitalisation (WHO,2022).
2. A decentralised model of care is recommended over a centralised model for patients on MDR-TB treatment
3. Uganda uses a mixed care model, with MDR TB isolation units at regional hospitals and ambulatory care at general hospitals with limited space. Patients needing stabilization should be referred to MDR TB centres, with admission limited to 2 weeks unless extended care is advised by the health worker.

Decentralised care: Decentralized care is defined as care that is provided in the local community where the patient lives at non-specialized or peripheral health centres, by community health workers or nurses, non-specialized doctors, community volunteers or treatment supporters. Centralized care is defined as inpatient treatment and care provided solely by centres or teams specialized in drug-resistant TB until the patient is stabilized. Afterwards, patients can receive decentralized care. In some early studies, improved treatment success and loss to follow-up has been reported for decentralised care versus centralised care. However, most recently (WHO),2022) ,early ambulatory care has been recommended over specialized care for improved patient outcomes and quality of life. There are scenarios when decentralised care is not appropriate such scenarios include patients with severe TB disease, patients with extremely infectious forms of the disease, patients with serious comorbidities or patients for whom treatment adherence is a concern. For such patients, it is recommended that they are stabilised before discharge into ambulatory care with appropriate supportive care ensured. Patients being managed in an outpatient setting, it is important that measures are put in place to protect their safety especially when regimens containing new or novel medicines are given.

## CHAPTER 5: COMMUNITY TB

Any undetected TB case in the community has potential to transmit TB to 10-15 individuals annually. Interventions that leverage lower-level health systems and community level structures have potential to identify TB patients in the community and ultimately cut the cycle of transmission in the community. Further, such interventions will lead to early TB diagnosis, prompt TB treatment initiation and lead to improved TB treatment outcomes. The community health care system that deploys community health workers could be supported and used to deliver activities critical to community TB care. The activities include:

### Community sensitisation about TB.

Community sensitisation is aimed at creating awareness and creating demand for TB services in the community. The sensitisation should cover important aspects of TB e.g., cause, spread, signs and symptoms and treatment. The sensitisation drive could be done at preselected venues within the community. The key steps include:

- Select location for the sensitisation activity. The selection is informed by the available data or information. The data available should be able to indicate communities where the high-risk groups are. Once the community where the sensitisation drive has been identified, a suitable venue for the drive should be selected. The community resource persons can help select such a place, but this place should be accessible and conducive for the activity.
- Obtain formal clearances. These are needed to ensure the activity is supported and well received in the community. The clearances could come from ministry and political leadership e.g., local council (LC) office.
- Contact and engage the community resourceful persons. These persons include the community health care workers, linkage facilitators, local area leadership (LC1), religious/spiritual and cultural leaders, VHTs and other community stakeholders.
- Prepare the required tools. All the necessary tools needed to support the sensitisation should be prepared in advance. Such tools include TB brochures, registers, referral forms, sputum collection logistics (sputum mugs, zip lock bags, cool boxes, cotton wool).
- Community mobilisation. The community should be mobilised to come for the sensitisation drive. The mobilisation should be done in collaboration with the resourceful persons. Mobilisation can be done through community radios, public address systems (megaphones), flyers, banners among others. Engage other community stakeholders including CSOs and CBOs at the community level in the mobilisation drive.
- Offer TB screening services and provide the necessary guidance for service provision. At the venue, the participants should be screened for TB using the screening tests available. Those found presumptive should be investigated further.

### Distribution of TB information, education, and communication (IEC) materials.

The following are the steps for conducting this activity.

- Identify areas and people that need and should be given the IEC. The areas/people include health facilities, communities, community leaders among others. The actual IEC materials needed are then agreed upon.
- Contact the community resource team (VHT, LCI executive, social workers, CSOs and CBOs etc) within the community to help with scheduling the distribution of the materials. The resource persons will help identify the best distribution channels
- Ensure that the required materials are available for distribution in sufficient quantities and in languages the individuals can understand

- At the point of distribution, the responsible individual should explain the information in the materials using a language that is easy to understand
  - Allow for questions about the materials and ensure all questions are answered
  - The personnel distributing the materials should share contact information for future consultation in case the individual wants to consult further
  - As much as possible, obtain materials that have been translated into the local language of the area where they will be distributed
1. Contact tracing. Contact is a risk for TB disease and it's important all individuals with established contact with the diagnosed TB patient are identified and screened for TB disease. The following is the approach to conducting TB contact tracing.

### **At the health facility**

- Health care workers should identify and list all index TB patients registered in care
- Listing all close contacts of the index TB patient. Contacts could be within the household, workplace or school. The listing should be done by the health care workers in consultation with the client. The health care worker should establish a good rapport with the TB patient and help them understand why it's important contact tracing is done. The listing should capture enough contact information including physical addresses to allow for locating of the contacts
- The health care worker should seek the consent of the clients to visit their household/workplace contacts. This consent can be verbal.
- Ensure you have all the required tools (e.g., job aids, registers, sputum mugs, adherence counselling forms.) and logistics for contact tracing
- Working with the index TB patient, schedule appointments for the visit

## In the community

- Explain to the contact the reason you are visiting them and the procedures involved
- Using the available tools e.g., the TB/HIV flip chart, educate the contacts on TB. Also ask them if they have any unanswered questions and give them the answers
- Screen the contacts for TB. Using the ICF, screen the contacts, one contact at a time
- Record the findings from the assessment of each contact into the contact screening register
- All contacts screened who are positive for any of the TB symptoms in the ICF should be recorded in the presumptive register. Those who test positive for TB should be tested for HIV.
- Guide the presumptive TB patient through the sputum collection procedure and pack the sputum safely. Fill the laboratory request form with the needed details. The collected sputum sample should be packaged appropriately and transported to the health facility for laboratory staff for testing. If the patient is unable to provide a sample at that time, give them the sputum mug and instructions on how to produce a high-quality sample and agree on where they should take the sample for testing. The participants with non-cough symptoms should be guided on how to produce a sample. Those that fail should be referred to the health facility for further assessment
- The health care worker, VHTs and other players conducting the contact tracing should check with the health facility at least weekly to establish if all presumptive TB cases/ patients referred reached the facility.
- The health care worker, VHTs and other players conducting the contact tracing should follow up with the referred presumptive cases to ensure they get tested and update the presumptive register with the results. If the client is found to have TB, they should ensure they get TB treatment and if negative, follow up for any further analysis should be done

## Targeted TB screening in congregate settings.

Congregate settings are good grounds for continued TB transmission and should be prioritised in community TB case finding programs. Congregate settings usually have many people living together and the living conditions normally predispose top TB infection and disease. These settings include prisons and penitentiary institutions, slums, refugee camps, schools among others. Key steps in performing this activity include:

## Planning

- Identification of the congregate setting
- Establishing contact with the authorities in the congregate setting identified. The authorities could include and administrative and political leadership. The aims of the activity and the plan (date, time, space for screening) should be explained to the authorities and clearance and support obtained
- Assembling screening team. A multidisciplinary team should be put together to oversee the activity. The team could include health care workers (clinicians, nurses, radiographers, laboratory technicians/technologists, VHTs, counsellors and TB survivors) and resourceful persons in the community. The roles and responsibilities of each member should be well defined.
- Logistics. Identify all the materials needed to conduct a successful TB contact screening activity and ensure there are enough supplies. The logistics include flyers, screening cards. Contact screening registers, sputum. Mugs, sputum packaging materials, referral cards, transport among others. CSOs should be included in the planning phase.

## **At the venue**

- Arrange the venue for easy client flow. Label places e.g., sputum collection area, screening area, etc. if needed
- Once at the venue, clearly explain to the clients what the activity is all about and manage their expectations.
- Conduct TB screening of the clients. The ICF guide can be used to assess the clients for TB
- Recording and reporting. Every patient screened should be entered in a screening register, those found presumptive for TB should be registered in a presumptive TB register
- Sample collection. All presumptive TB patients should be given sputum mugs and availed sufficient instructions to be able to produce a high-quality sputum sample. If the sample cannot be collected at that time, the client should be given the sputum mug and a referral form and guided on where they should take the sample for testing
- Testing the collected samples. All the sputum samples collected should be well packaged and transported to the health facility for laboratory testing. The samples should be submitted to the laboratory together with the test request forms.
- Follow up should be done to ensure the patients found positive for TB are initiated on TB treatment and those negative but qualify for TB preventive treatment (TPT) according to the TPT guidelines are receive the treatment. Those that are diagnosed with TB should have an HIV test

## **TB treatment adherence, assessment and planning.**

TB treatment adherence is key to successful TB treatment outcomes and thus needs to be emphasized for all patients initiated on TB treatment. The health care workers should assess for adherence and ensure any potential factors likely to lead to poor adherence are addressed. This activity could be conducted as part of the differentiated service delivery models for TB. The steps to conducting this activity are as follows:

- Patient education. Educate all the patients being initiated on treatment on why adherence is important. They should be informed of the potential side effects of the drugs, how to recognise them and manage them. They should also be informed of where and how to get help when they encounter the side effects. The need for patients to continue treatment even after they feel better should be emphasized.
- Use tools to monitor and assess adherence. Various tools are used to monitor adherence. The easiest tool to use is the patient card. The others include counting the number of pills that should have been taken up to the time the assessment is done. Also, the tablets should be checked to ascertain storage conditions. Ask the patient to explain how they have been taking the drugs.
- Other tools that could be used to monitor and ensure adherence and include digital adherence technologies like use of phone calls, video assisted directly observed treatment, 99 DOTS among others.
- In case during the adherence assessment, it emerges there are adherence issues, then the patient has adherence problems and an adherence risk assessment is needed.
- Conduct the risk assessment and record the findings on a risk assessment tool
- Identify issues leading to poor adherence in the patient assessed
- Working with the patient, agree on action plans and strategies for supporting adherence. At this time, reemphasize the benefits of TB treatment and dangers on non-adherence
- Document the agreed action plans in a TB treatment adherence plan form
- Follow up with the patient to ensure they are following the action plans agreed upon. This can be through a phone call or physical visit to the patient. Other important players such as VHTs, CSOs, CBOs could be leveraged to support this.

## Sputum sample collection and transportation

Community sputum sample collection and transport to testing facilities must follow proper procedures

- Logistics. Ensure all the needed tools and materials needed are available. These could include sputum mugs, cotton, gloves, Ziplock bags, cool boxes, masks, laboratory request forms, referral forms, transport etc.
- In the community, educate the individual why you are collecting their sample and why they should give a good sample for testing.
- Provide the individual with clear instructions to ensure a quality sputum sample. Sputum should be collected in a separate area, preferably outdoors, using a wide-mouthed, leak-proof container with a lid. Instruct the individual to cough and produce 3–5ml of sputum, ensuring it is mucoid, mucopurulent, or purulent. For those unable to produce a sample, simple manoeuvres like taking a walk may help.
- Label the sputum container clearly with the individual's details before the sample is put in the container. The Ziplock bag must also be labelled
- Complete a laboratory request form for each sample, ensuring the details match the sample and form.
- Use triple packaging to secure the sample and transport it to the testing facility.
- Transport the samples to the testing facility where documentation of all the samples delivered will be done through use of a sample tracking log. This will be signed by the laboratory/health care workers on delivery of the sample.

## Follow up of missed appointments and lost to follow up TB patients

Adherence to treatment plans is vital, and healthcare workers must follow up with patients who miss appointments or are lost to follow-up. The process is outlined below:

- Prepare a list of all patients that have missed their appointments or are lost to follow up. This should be done in liaison with the health facility staff. The line list should have all the required contact information of the patient i.e., telephone and physical address. The next of kin contacts can be obtained too.
- Schedule the follow up visit to the lost patients and those that missed their appointments
- For those with phone contacts, establish contact with the participant and ascertain reasons for their missed appointments and any challenges with adhering to treatment
- On the visit to the community, ensure all the tools needed for adherence assessment, counselling, self-management/adherence planning are available. The tools include contact tracing form and referral form among others.
- Through interaction with the patient, establish the reasons for missed appointment or lost to follow up. Work together with the patient and agree on an action plan and document this on the adherence plan form. Before leaving the patient, check that they have understand the plan
- Provide feedback to the health facility about the follow up activity.

## Supporting community based directly observed therapy (CB-DOT)

Healthcare services should be decentralized, family-centred, and delivered with minimal patient inconvenience, supported by approaches like differentiated service delivery models (see DSD section).

## CROSS BORDER TB/LEPROSY MANAGEMENT

Cross-border TB management aims at addressing mobile key populations like travellers, refugees and nomads.

The activities conducted include:

1. Coordination with the neighbouring countries to improve TB services in the border areas
2. Tracking of patients across borders to ensure continuity of TB treatment
3. Helping health facilities in the border districts to get contacts of their counter parts in the neighbouring districts for easy data exchange and validation on TB patients that cross borders
4. Ensuring that TB screening is done at Points of Entry (POEs) for all the travellers passing through the gazetted POEs.

### **How to conduct TB screening at the POEs**

Uganda has 53 official POEs. Some of these POEs have established structures and staffing: the health facility (Port health) in charge, laboratory technologist, nurses and environmental health assistants. These are employed by the respective district local governments where the POEs are located. TB screening activities will leverage the existing work force and integrate the screening activities into other activities done by these port health units.

Screening for active TB at POEs ensures that active TB including drug resistant TB are detected early and treatment is initiated promptly.

This will ultimately reduce the risk of poor treatment outcomes, health sequelae and the adverse social and economic consequences of TB as well as help reduce TB transmission. This also helps identify the would be missed TB patients.

### **Target population for TB screening at the POEs**

The following will be the target for the screening at the POEs:

- Truck drivers and their turn boys
- Businessmen/women
- Tourists
- Immigrants, refugees
- All other persons passing through the gazetted POEs

### **Screening Procedure**

All relevant stakeholders will be introduced to the concept of TB screening at the POEs. Once this is done, the necessary tools will be availed to the POE team to facilitate TB screening.

- i. TB screening will be done by health workers and immigration officers at the respective POEs using a guide provided by National TB and Leprosy Program
- ii. Every traveller will pass through the health unit to be screened for TB as part of clearance at the border
- iii. The Intensified Case Finding (ICF) stamp will be used to confirm that a particular traveller has been screened for TB
- iv. Any person who is presumed to have TB will be required to give us a sputum sample in appropriate sample collection containers to enable safe sample transport

- v. All presumptive TB patients will be recorded in a Presumptive TB register and their phone contacts captured. After sample collection the passenger will then proceed with his or her journey
- vi. TB samples will be triple packaged and referred to the nearest GeneXpert site through the hub system. The nearest GeneXpert site will run samples and results will be returned to the POE by the Hub riders
- vii. POE Health workers will also be required to follow with the GeneXpert sites for results of all referred samples on a weekly basis and report on the proportion of referred samples for which results were returned
- viii. The district laboratory TB focal person (DLFP) in conjunction with the port health in charge and the laboratory technician will be responsible for management of laboratory processes at POE and GeneXpert sites
- ix. Results will be relayed to the owners using the contacts recorded and nearest health facilities/districts for Ugandans and respective border officials for the corresponding country for foreigners
- x. Travellers/patient found positive with TB will be linked to the nearest health facility for treatment initiation. For those travellers already on TB treatment, they will be linked to health facilities nearest to them to ensure continuity of treatment for better treatment outcomes and follow up sputum examinations are done
- xi. Any presumptive TB patient who is not able to give a sputum sample on the spot will be advised to go to the health facility nearest his/her destination for more clinical evaluation
- xii. No traveller/ passenger will be stopped from proceeding with his/her journey even when he or she is presumed to have TB.

*Table 27 Stakeholders and their roles in PoE TB screening*

Stakeholder	Role
NTLP	Provision of guidelines on TB screening at the POEs
	Organising orientation on TB screening at the POE
	Provision of tools such as presumptive TB registers
	Coordination with the ministries, departments and agencies (MDAs) and neighbouring countries
DHO's office (DHO, DTLS, DSFP, DFLP)	Ensures that TB screening and reporting of data at the POE is done
	Deployment of health workers to screen for TB at the POE per the guidelines
	Coordination of implementing partners (IPs) supporting the POEs
	The DLFP in conjunction with the port health in charge is responsible for management of laboratory processes at POE and GeneXpert sites
Port health in charge	Ensures that TB screening at the POE is done
	Ensuring that sputum samples are referred to the laboratory and results relayed to their owners
	In conjunction with the DTLS, ensure that TB patients are linked to treatment sites
Head of immigration at the POE	Ensure that all travellers are screened for TB before they are cleared by the immigration officers
Head of customs at the POE	Ensures that the traveller is screened for TB before he/she is cleared by the customs officers
Security (Police, army, border internal security officer- BISO)	Ensure that health workers and other TB screeners are working within a secure environment with no threats of violence from the travellers
Implementing partners (IPs)	In conjunction with different stakeholders provides the addition support for TB screening, sample referral and linkage of patient to treatment sites

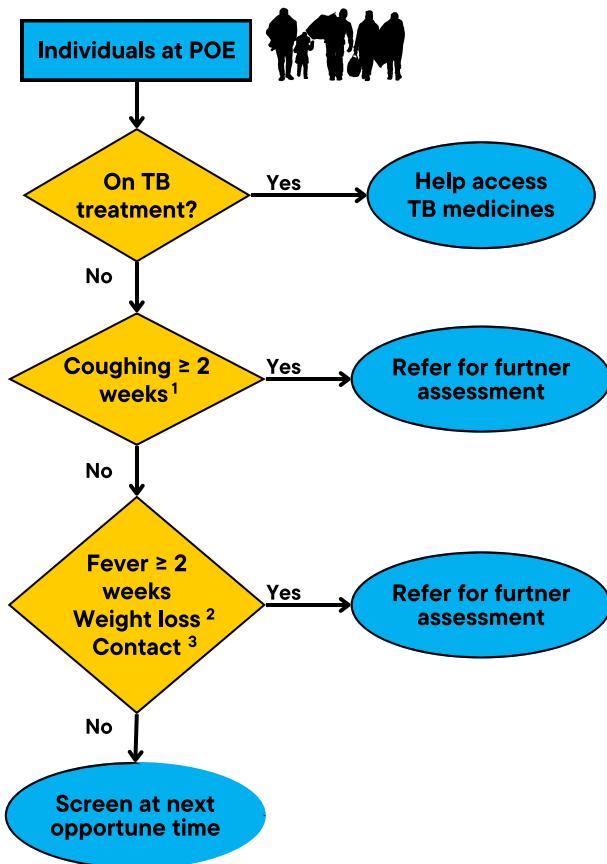
## Screening questions for use at the points of entry/exit at the Ugandan designated border points

These guiding questions should be administered by a health care provider or lay provider such as immigration officer at the border points

Table 28 Questions to ask at POEs

1	Has the traveller been coughing for two weeks or more (for HIV known patient/traveller assess for any duration)?	Yes	No
2	Has the traveller had persistent fever for two weeks or more?	Yes	No
3	Has the traveller had noticeable weight loss (more than 3 Kgs) or poor weight gain for children?	Yes	No
4	Has the traveller had any close contact with a patient of TB OR any person with long standing cough	Yes	No
5	Is the traveller on medication for TB?	Yes	No

Figure 18 Procedure for screening at POEs



- 1.Cough of any duration for known HIV patient or traveller
- 2.Weight loss of at least 3kg or poor weight gain in children
- 3.Close contact with TB patient or person with a longstanding cough

## Reporting of cross border TB services

TB screening data at POEs is reported through the electronic integrated disease surveillance and reporting (eIDSR) system. This is a daily report submitted to the surveillance unit of the MOH. The NTLP gets weekly aggregate reports for further analysis and action.

Districts are expected to track TB patients on treatment that have crossed over to the neighbouring countries to ensure treatment completion and outcomes are documented. Each health facility should have a line list of patients referred across borders or suspected to have crossed over the borders that need follow up and update the records. Each border district should have a directory for all facility in-charges and district/county TB and leprosy supervisors in the neighbouring country for easy coordination.

## CHAPTER 6: POST TUBERCULOSIS LUNG DISEASE

The public health impact of post-TB lung disease (PTLD) is increasingly recognized, with emerging guidelines for its evaluation and treatment. Chronic respiratory symptoms, such as chest pain, cough, shortness of breath, wheezing, and haemoptysis, affect up to half of patients previously treated for TB. These individuals are at high risk of recurrent TB, with significant residual morbidity and mortality even after successful treatment. In Uganda, studies show a high prevalence of COPD and poor quality of life among MDR TB treatment completers.

Globally, 41% of TB survivors experience PTLD, defined as chronic respiratory abnormalities partly attributable to previous pulmonary TB (PTB). Clinically significant PTLD involves respiratory symptoms likely caused by prior PTB and not explained by other conditions (e.g., asthma, COPD). Patients often present with persistent symptoms, reduced lung function, and impaired work capacity. Managing PTLD requires avoiding conventional TB treatment and enhancing screening pathways for recurrent PTB.

PTLD results from the direct effects of *M. tuberculosis* and the host immune response, causing airway distortion, reduced elasticity, and damage to lung structures. These changes manifest as structural abnormalities on imaging and reduced lung function on spirometry.

### Clinical presentation of PTLD

Post TB disease presentation could range from asymptomatic to debilitating illness. Multiple patterns of pathology can be seen within a single patient, between or within areas of the lung. Table 29 below shows the several ways PTLD could present.

*Table 29 Presentation of Post TB lung disease*

Compartiment	Clinical patterns	Suggested definition
Airways	Tuberculosis-associated obstructive lung disease	Airway obstruction (FEV1/FVC ratio <0.7) thought primarily related to small airway disease
	Bronchiectasis	CT definition – evidence of airway dilatation > diameter of adjacent vessel, or non-tapering, or CXR definition – evidence of ring shadows and tramlines
Parenchyma	Cavitation	A gas-filled space either within an area of pulmonary consolidation or surrounded by a thin wall
	Parenchymal destruction	Extensive destruction of lung tissue, with a gas-filled space/collapsed parenchyma occupying the volume of $\geq 1$ 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	
Pulmonary vascular	Pulmonary hypertension	Elevated pulmonary artery pressures, as estimated using Doppler echocardiography or measured at right heart catheterisation

PTLD, post-tuberculosis lung disease; FEV1, forced expiratory volume in 1 second; FVC, Forced vital capacity.

CT, computerized tomography; CXR, chest radiograph

## Management of Post TB Lung disease

Management of post TB lung disease is guided by clinical standards. The clinical standards are described below.

### Clinical standards for the assessment, management and rehabilitation of PTLD

#### Standard 1: Every patient completing TB treatment should be clinically evaluated for PTLD.

The assessment should be conducted as soon as possible at the end of treatment and organised by the TB programme. The following basic examinations are essential upon clinical suspicion of either the presence of, or risk factors for, PTLD: history taking and clinical examination, Chest Xray, pulmonary function testing (PFT), six-minute walking test (6MWT). These exams/tests need to be complemented by symptom score and Quality of Life (QoL) questionnaire evaluation.

Bacteriological results (sputum smear microscopy and culture) are important at diagnosis, during follow-up and at the end of treatment to determine the TB treatment outcome (cured or treatment completed)

*Table 30 Recommended examinations to be conducted at the end of treatment*

Essential and conditional examinations/investigations		Adaption for special settings and situations
Clinical assessment	Clinical history, symptom assessment and clinical examination	Clinical history, symptom assessment and clinical examination
Imaging	(i) Chest radiography (digital) (ii) Computed tomography	Chest radiography
Functional evaluation	(i) Spirometry, including pre- and post-bronchodilator test (ii) Plethysmography (iii) Diffusion capacity assessment (DLCO, KCO) (iv) Tidal breathing techniques (oscillometry/MBW) (v) Arterial blood gas analysis, and pulse oximetry (SpO2) (vi) 6MWT (vii) CPET	(i) Spirometry (ii) SpO2 (iii) 6MWT
Subjective evaluation	(i) QoL questionnaire (ii) Frequent symptoms score	(i) QoL questionnaire (ii) Frequent symptoms score

DLCO=diffusing capacity of the lungs for carbon monoxide; KCO=carbon monoxide transfer coefficient; MBW=multiple breath washout; SpO2=peripheral capillary oxygen saturation; 6MWT=six-minute walking test; CPET=cardiopulmonary exercise testing; QoL=quality of life

\*The tests above can also be performed in special cases, such as for former TB patients, even months after completing treatment, if necessary.

The six-minute walking test (6MWT), following international guidelines, is a simple, reliable, and resource-efficient tool to assess exercise capacity, prognosis, and treatment response in chronic respiratory diseases.

Persistent symptoms like breathlessness or cough indicate disease progression, reducing physical function and quality of life (QoL). Although not specific to PTLD, validated questionnaires for chronic respiratory diseases can assess QoL, with the choice depending on available time and patient education level.

**Standard 2: Evaluation for Pulmonary rehabilitation**

Former TB patients with clinical and radiological signs and symptoms consistent with post-TB treatment sequelae, evidence of obstruction and/or restriction, desaturations and/or low oxygen levels, reduced exercise tolerance and related impairment in quality of life should be evaluated for PR.

There is strong evidence that PR improves health status, exercise capacity, fatigue, and social functioning, and is recommended in international guidelines

After excluding cardiovascular risks, PR is an appropriate measure for patients with persistent symptoms (dyspnoea, chest pain, cough, muscular fatigue), or reduced exercise tolerance, a restriction in activities because of their disease, exercise-induced oxygen desaturation, or impaired health status.

A comprehensive assessment should be performed in order to identify and quantify possible impairment due to PTLD (Table 21 above). The assessment should focus on TB sequelae and their functional impact, as well as on pulmonary interventions needed. PR is a comprehensive package of interventions, which can include exercise, education, nutrition, self-management activities and psychosocial support.

**Standard 3: The PR programme should be organised according to feasibility, effectiveness and cost-effectiveness criteria, and should be tailored to the individual patient's needs.**

To qualify as PR, programmes must include, at the very least, comprehensive baseline and post-PR outcome measurements, a structured and supervised exercise training programme, an education/ behavioural programme, and provision of recommendations for home-based exercise and self or supervised physical activity programmes.

Table 31 Summary of the core components of a rehabilitation programme

Components	Indication	Methods	
		Interventions	Adaptation to special setting and situations
Aerobic exercise: endurance training	<ul style="list-style-type: none"> <li>Impaired exercise capacity, limited by dyspnoea and or other respiratory symptoms</li> <li>Restriction in daily life activities</li> </ul>	<ul style="list-style-type: none"> <li>Treadmill and/or cycle-ergometer</li> <li>30 min 2–5 times/week for 4–8 weeks</li> <li>Intensity set according to maximal oxygen consumption or the equation of Luxton or 80% of heart rate max adjusted on dyspnoea</li> <li>In or out-patients or tele-monitoring</li> <li>Suggest maintenance programme</li> </ul>	<ul style="list-style-type: none"> <li>Free walking</li> <li>30 min 2–5 times/week for 4–8 weeks</li> <li>Intensity set according to perceived dyspnoea</li> <li>Outpatients or home setting</li> <li>Suggest maintenance programme</li> </ul>
Airway clearance techniques	<ul style="list-style-type: none"> <li>Difficult to remove secretions or mucous plugs</li> <li>Frequent bronchial exacerbations (<math>\geq 2/\text{year}</math>)</li> <li>Concomitant diagnosis of bronchiectasis</li> </ul>	<ul style="list-style-type: none"> <li>Choose the technique suitable for the subject among those available, based on respiratory capacity, mucus rheology, collaboration and patient preferences</li> <li>15–30 min one or more times/day</li> <li>Choose the duration of treatment based on chronic (long term) or acute problem (short term)</li> <li>Suggest maintenance programme when needed</li> </ul>	<ul style="list-style-type: none"> <li>Choose the technique suitable for the subject among those available, based on respiratory capacity, mucus rheology, collaboration and patient preferences</li> <li>15–30 min one or more times/day choose the duration of treatment based on chronic (long term) or acute problem (short term)</li> <li>Suggest maintenance programme when needed</li> </ul>
Nutritional support	<ul style="list-style-type: none"> <li>Malnutrition (body mass index <math>&lt;16 \text{ kg/m}^2</math> or body mass index <math>&lt;17 \text{ kg/m}^2</math> in patients with TB-HIV, MDR-TB, or pregnant and lactating mothers)</li> </ul>	<ul style="list-style-type: none"> <li>Nutritional assessment</li> <li>Tailored treatment from foods and medical supplements</li> <li>Need for financial incentives, and transportation access should be evaluated</li> </ul>	<ul style="list-style-type: none"> <li>Nutritional assessment</li> <li>Tailored treatment from foods and medical supplements</li> <li>Need for financial incentives, and transportation access should be evaluated</li> </ul>
Psychological support	<ul style="list-style-type: none"> <li>Social isolation, depression and anxiety. Impaired health status and/or quality of life despite optimal pharmacological treatment.</li> </ul>	<ul style="list-style-type: none"> <li>Psychological assessment</li> <li>Psychological support</li> <li>Consider self-help group</li> </ul>	<ul style="list-style-type: none"> <li>Psychological assessment</li> <li>Psychological support</li> <li>Consider self-help group</li> </ul>

#### Standard 4: Evaluating the effectiveness of PR for former TB patients

Evaluation of effectiveness of PR is done by comparing the core variables before and after rehabilitation. As a minimum, the patient's functional exercise capacity, dyspnoea and health status should be assessed. The measure of exercise capacity most frequently used is the 6MWT, but the cardiopulmonary exercise test or the incremental shuttle walk test and the 5 repetition sit to stand test are also applied.

PR in PTLD patients has been shown to significantly improve the distance covered during the 6MWT (by approximately 35–45 m).

**Standard 5:** Each patient completing PR should undergo counselling/health education, including a follow-up plan to maintain/improve the results achieved, organised according to feasibility and cost-effectiveness criteria, and tailored to the individual patient's needs.

**Standard 6:** Each change in outcome for a patient (cured or treatment completed as per WHO guidelines) occurring during or after PR should be promptly notified to public health services and be included in the TB register.

## CHAPTER 7: TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

### Introduction

Children and adolescents under 15 years contribute 12% of global TB cases, equating to 1.25 million annual cases, nearly half under age five. Many are missed due to nonspecific symptoms, challenges in specimen collection, the paucibacillary nature of TB in young children, and limited access to sensitive point-of-care tests. Additionally, only a third of child TB contacts under five eligible for TB preventive treatment (TPT) received it in 2024.

Older adolescents (15–19 years) account for about 500,000 TB cases annually and are a key transmission group due to high social mobility and disease infectiousness. Young children are at greater risk of severe TB forms, often within months of exposure, due to their underdeveloped immune systems. Severe cases, such as disseminated TB or TB meningitis, are more common in children under two years.

In Uganda, children aged 0–14 years represent 16% of notified TB cases, with an increase in both incident and clinically diagnosed cases over recent years. Childhood TB, typically primary, signals ongoing community transmission from infectious adults or older children, particularly those who are smear-positive and untreated. Rarely, children may acquire TB congenitally or through unpasteurized milk (Bovine TB).

Adolescents often present with adult-type TB (e.g., cavities on chest X-rays and bacteriological confirmation) and require specific support for adherence and transitioning from paediatric to adult healthcare systems.

### Risk factors for TB

#### Risk factors for TB infection

The risk factors for TB infection include: -

- a) Contact with an infectious TB case (source case). The risk of infection is greater with:
  - close contact
  - prolonged duration of contact.
  - bacterial load of source case
  - poor ventilation
- b) Increased exposure in community: Individuals who live in high TB endemic communities are more likely to have TB infection than those in low TB endemic communities.

#### Risk factors for TB disease

- a) Once exposed to a person with PTB disease, the following are risk factors for developing TB disease in children:
- b) Young age: Children under 2 years are at higher risk of developing TB and severe forms of the disease upon exposure.
- c) HIV infection
- d) Severe malnutrition particularly undernutrition
- e) Severe malnutrition is associated with impaired cell mediated immunity thereby predisposing to TB disease.
- f) Recent episode of measles, pertussis
- g) Measles is associated with a weakened immune system that puts a child at risk for developing TB disease.
- h) Other immunosuppressive conditions e.g., diabetes, children on chemotherapy, prolonged steroid use

## **Risk factors for severe TB disease**

- a) Young age: Children under 2 years are at higher risk of developing TB and severe forms of the disease e.g.TB meningitis.
- b) Lack of BCG vaccination: BCG vaccination is more effective against severe forms of TB particularly TBM

## **Diagnostic approach**

Most children with TB present with non-specific signs and symptoms making the diagnosis of TB in children dependent on consideration of findings from TB symptoms screening (including history of contact), clinical examination and relevant tests. The approach to diagnosis of TB in HIV infected children is similar to that in HIV uninfected children.

Diagnosis of TB in young children is associated with:

- i. paucibacillary disease, implying that they harbour relatively few TB bacilli, and thus diagnostic tests that detect TB bacilli are not as sensitive in young children as in older adolescents and adults with TB
- ii. challenges in sputum sample collection. The use of alternative sample types, such as stool, that can be collected in a less invasive way is important for obtaining bacteriological confirmation

All children and adolescents that are identified with presumptive TB should be evaluated further for TB disease.

## **Screening**

Screening options available include symptom screen, chest Xray for contacts of TB patients and CRP for PLHIV above 10 years. Additionally, the CXR is a useful part of a diagnostic evaluation for TB in all children, including those living with HIV, especially younger children in whom bacteriological evaluation is commonly negative.

TB symptom screening should be conducted using the ICF guide (*Figure 5*).

The following are the commonest symptoms of TB in children and therefore if any child presents with any, he or she has presumptive TB.

- i. Persistent cough for two weeks or more OR current cough with any of the symptoms listed below
- ii. Prolonged fever for 2 weeks or more, with or without night sweats
- iii. Weight loss or poor weight gain or failure to thrive for 2 weeks or more: defined as weight loss, or very low weight (weight-for-age less than -3 z-score), or underweight (weight-for age less than -2 z- score), or confirmed weight loss (>5%) since the last visit, or growth curve flattening, or Mid Upper Arm Circumference (MUAC) measurement in the yellow or red colour code
- iv. History of TB Contact
- v. Poor appetite or anorexia
- vi. Fatigue or reduced playfulness, poor feeding or reduced activity in the presence of any of the above symptoms

Other symptoms of TB could include: painless enlarged cervical lymph nodes, Gibbus, haemoptysis in older children and adolescents. The presentation of TB in adolescents is similar to that in adults.

All children and adolescents meeting the criteria for presumptive TB, should undergo further assessment for TB that includes clinical examination and relevant TB tests.

## **Detailed history taking**

Conduct a detailed history including history of TB exposure. History of exposure should not only be limited to the household members but include the persons the child has been in contact with outside the household. If the child has a positive history of TB exposure, it is important to establish whether the person with TB has drug susceptible or resistant TB. History taking also provides an opportunity to assess for other disease conditions which may present like TB.

## **Clinical examination**

Assess for the following:

- i. Poor weight gain – check and record weight and compare with previous weight in the past 3 months. Look for weight loss and check for growth faltering or failure to thrive
- ii. Vital signs – check for elevated temperature (fever) and increased respiratory rate
- iii. Signs of respiratory distress such as chest indrawing, stridor and oxygen saturation below 90%, abnormal auscultation and percussion sounds, or signs of a pleural effusion (dullness, reduced breath sounds).
- iv. Other physical signs suggestive of PTB include: – severe acute malnutrition not responding to therapeutic nutritional treatment; acute pneumonia not responding to adequate course of antibiotics; persistent wheeze not responding to bronchodilators and lymphadenopathy
- v. Physical signs suggestive of EPTB

## **Relevant investigations**

### **Laboratory tests**

Although bacteriological confirmation of TB in children is not always possible, it should be sought for whenever possible. The mWRDs are the recommended initial TB diagnostic tests for children and adolescents, a recommendation that is similar to adults. Stool testing using the simple one step processing method should be used when available. It is important to note that Complete Blood Count (CBC) and Erythrocyte Sedimentation Rate (ESR) are nonspecific and are not recommended as part of routine investigations used in the diagnosis of TB.

Samples for TB testing include:

- PTB: sputum (expectorated or induced), gastric aspirates, nasopharyngeal aspirates, stool.
- EPTB: lymph node aspirate, cerebrospinal fluid, pleural fluid, ascitic fluid

## **Radiology**

### ***Chest X-ray (CXR):***

The CXR remains an important tool in the diagnosis of TB in children, especially those with negative bacteriological tests or where bacteriological testing is not available or not feasible. If available, anteroposterior and lateral films should be obtained in children aged under 5 years, and posteroanterior films in older children and adolescents. Children with high-risk health should access X-ray services where available.

Abnormalities on CXR suggestive of PTB include:

- Enlarged perihilar or paratracheal lymph nodes;
- Dense alveolar opacification in a child who is not acutely ill;
- Miliary pattern of opacification;
- Cavitation (more frequent in adolescents);
- Pleural or pericardial effusion in a child or adolescent who is not acutely ill.

Adolescents with TB usually have radiographic changes similar to those seen in adults, with apical infiltrates with or without cavity formation or unilateral large pleural effusions being the most common forms of presentation.

### ***Ultrasound scan:***

If available, ultrasound can be used to aid in the diagnosis of TB in children for example abdominal TB

## **TB diagnosis**

The decision to treat TB will be guided by the findings from screening, detailed history, clinical examination and relevant investigations. The TB diagnosis algorithm for children is used to make the TB treatment decision (Figure 15). All children with bacteriologically confirmed TB will be treated for TB. Where bacteriological confirmation is not possible or not obtained, the TB diagnosis algorithm will be used.

The decision to treat will be based on the following four criteria;

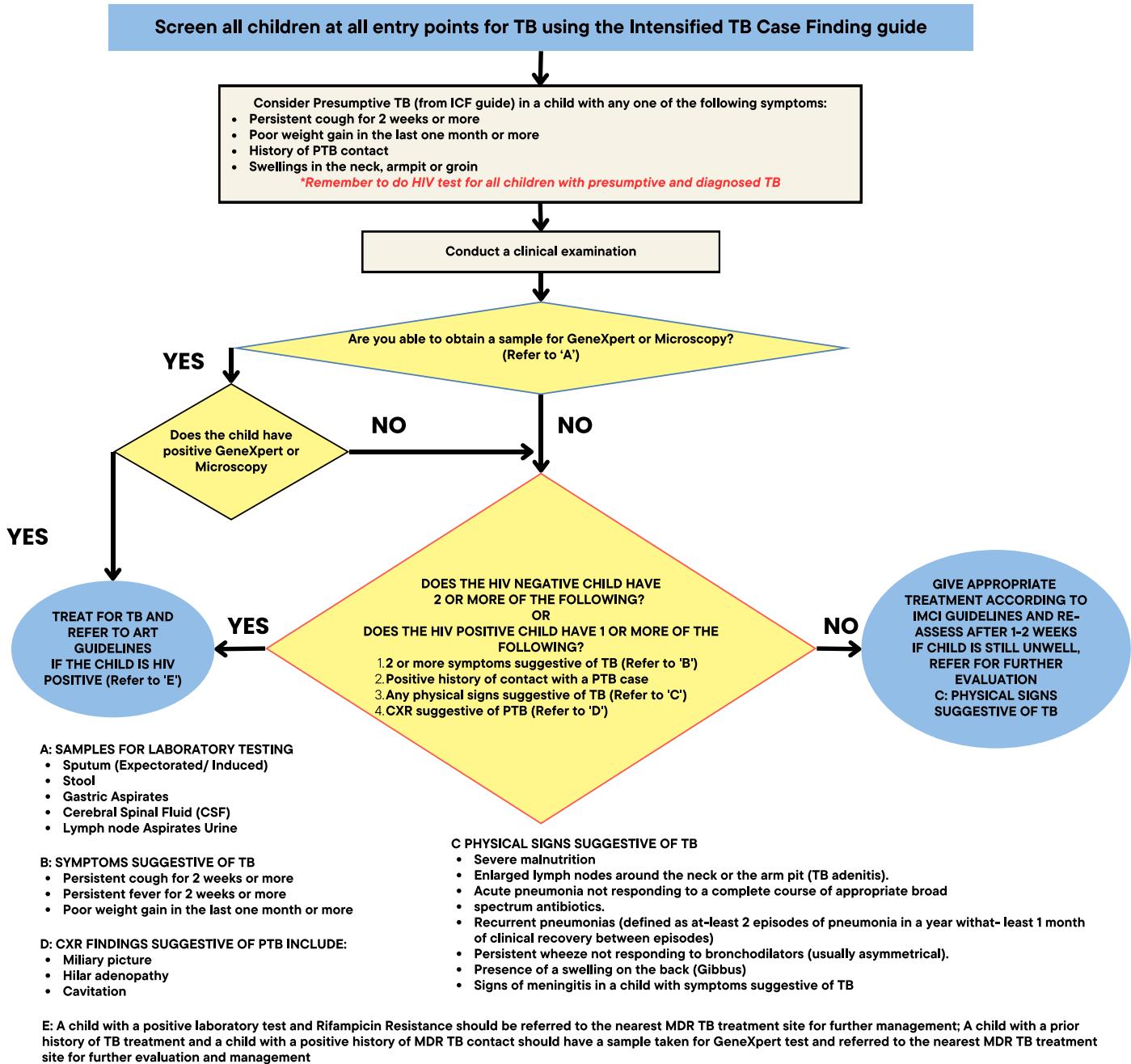
- A: 2 or more symptoms suggestive of TB
- B: Positive history of TB contact
- C: CXR suggestive of TB
- D: Physical signs suggestive of TB

**For HIV-negative children, the presence of any two criteria warrants treatment for TB.  
However, for HIV-positive children, just one criterion is sufficient to initiate TB treatment.**

Figure 19 Algorithm for the diagnosis of TB in children



## ALGORITHM FOR THE DIAGNOSIS OF TB IN CHILDREN



## Package of care for children and adolescents with advanced HIV disease

The Screen, Treat, Optimize and Prevent AIDS (STOP AIDS) package of care is a WHO recommended set of interventions for children and adolescents presenting with advanced HIV disease and has been adopted by MOH. The table below summarises the recommended interventions for screening, treating, optimizing ART and preventing advanced HIV in children and adolescents living with HIV.

*Table 32 Screening, diagnosis, treating and prevention components of the package of care for children and adolescents with advanced HIV disease*

Intervention	Component	<5 years	5–9 years	10–19 years
Screening	- Screen for TB using the TB ICF guide. Use Point of care CRP for adolescents in addition to the ICF form	Yes	Yes	Yes
	- Use the recommended screening and diagnostic algorithms for TB			
Diagnosis	- Use the following diagnostic tests to confirm TB Rapid molecular diagnostic tests e.g., Xpert® Xpert® Ultra, TRUENAT or TBLAMP assays as the preferred test using sputum (expectorated or induced), gastric aspirate, stool or nasopharyngeal aspirate or other extrapulmonary specimens. Lateral flow urine lipoarabinomannan (LF-LAM) assay	Yes	Yes	Yes
	- Use X-ray to aid TB diagnosis if available			
Treatment	- If/When diagnosed with TB, treat for TB according to the national treatment guidelines.	Yes	Yes	Yes
	- Treat other conditions as may be available e.g., severe pneumonia, severe bacterial infections, cryptococcal meningitis and severe acute malnutrition according to national guidelines			
Optimisation of ART	- Rapidly initiate	Yes	Yes	Yes
	- Optimal antiretroviral regimen i.e., within seven days			
Prevention through TB preventive treatment	- Antiretroviral therapy counselling	Yes	Yes	Yes
	- Co-trimoxazole to prevent severe bacterial infections and pneumocystis pneumonia			
	- TB preventive treatment as per the national guidelines	Yes	Yes	Yes

## Treatment of drug susceptible TB in children and adolescents

The principles and objectives of TB treatment are similar to those of adults (Chapter 5). In addition, effective treatment of TB in children and adolescents promotes growth and development.

TB medicines in children and adolescents are administered per kg body weight using weight bands and therefore the weight should be measured at treatment initiation and each time of TB medicines' refill.

## **Treatment of Pulmonary TB**

TB treatment in children largely mirrors that of adults, comprising two phases: \*\*intensive\*\* and \*\*continuation\*\*. The intensive phase rapidly kills TB bacilli to halt disease progression, transmission, and drug resistance. The continuation phase eliminates dormant bacilli to ensure cure and prevent relapse. Current treatment regimens for children include:

- i. **2RHZE/4RH:** This is the same regimen used in adults except the doses are much lower in children and are calculated based on a child's weight. The current formulations for treating TB children are child friendly and available as RHZ, 75/50/150 (fixed dose combination) and Ethambutol 100 as a single formulation i.e., RHZ + E for the intensive phase and RH, 75/50 (fixed dose combination) for the continuation phase.
- ii. **2RHZE/2RH:** The 4 months shortened regimen TB treatment regimen applies to children and adolescents aged between 3 months and 14 years with non-severe drug susceptible TB. The current formulations for treating TB children are child friendly and available as RHZ, 75/50/150 (fixed dose combination) and Ethambutol 100 as a single formulation i.e., RHZ + E for the intensive phase and RH, 75/50 (fixed dose combination) for the continuation phase.

### **Eligibility for the 4 months shortened regimen TB treatment regimen (2RHZE/2RH)**

#### **Shortened 4-Month TB Treatment Regimen (2RHZE/2RH)**

This regimen is recommended for HIV-negative children aged **3 months to 14 years** who meet **all** the following criteria:

1. Mild Symptoms: The child has mild symptoms and does not require hospitalization.
2. No Severe Malnutrition: The child is not suffering from severe malnutrition.
3. Negative TB Test: The child has a negative TB test result.
4. No Complications on Chest X-ray (CXR): If a chest X-ray is available, it shows no evidence of: Miliary TB pattern
5. Cavitation, Airway obstruction, Complicated pleural effusion

**Peripheral TB Adenitis:** Children with peripheral TB adenitis who meet all the above criteria are also eligible.

#### **Important Considerations for the Shortened Regimen (2RHZE/2RH):**

- The shorter 4 months regimen applies to children aged 3 months - 14 years
- Children with any of the following ARE NOT eligible for the 4-month regimen and should be treated with the 6-month regimen
  - infants aged under 3 months
  - adolescents above 14 years
  - HIV
  - SAM
  - positive laboratory test,
  - Symptoms that require hospitalization
  - CXR with miliary TB pattern or cavitation or airway obstruction, or complicated pleural effusion on CXR
- Children who have a history of TB treatment in the past 2 years should not be treated with the shorter 4 months regimen

## **Other regimens**

2HPZM/2HPM: In adolescents aged 12 years and over, the 4-month isoniazid, rifapentine, pyrazinamide and moxifloxacin (HPZM) regimen may be used as an alternative regimen when supplies are available. This will be gradually rolled out as supplies and fixed dose combinations (FDC) become available.

## **Treatment of EPTB**

### **i. TB adenitis**

Children with TB adenitis may be treated with the four months shorter regimen if they fulfil the criteria listed in the previous section. If the child does not fulfil the criteria for the 4 months shorter regimen, they us treated for 6 months. The current formulations for treating TB children are child friendly and available as RHZ, 75/50/150 (fixed dose combination) and Ethambutol 100 as a single formulation i.e., RHZ + E for the intensive phase and RH, 75/50 (fixed dose combination) for the continuation phase.

### **ii. TB meningitis**

The treatment options for TB meningitis in children are as follows:

- 6RHZEto This is the preferred treatment regimen for drug-susceptible TB meningitis and consists of Isoniazid, Rifampicin, Pyrazinamide, and Ethionamide administered for 6 months. If the formulations are not available, use the 12-month regimen listed below.
- 2RHZE/10RH: This is the alternative treatment regimen for drug-susceptible TB meningitis. and consists of 2 months of RHZE, followed by 10 months of RH for a total treatment duration of 12 months. Use this regimen if the formulations for the preferred regimen are not available. The current formulations for treating TB children are child friendly and available as RHZ, 75/50/150 (fixed dose combination) and Ethambutol 100 as a single formulation i.e., RHZ + E for the intensive phase and RH, 75/50 (fixed dose combination) for the continuation phase.

### **iii. Osteoarticular (Bone) TB**

2RHZE/10RH Children with osteoarticular TB should be treated with a four- drug regimen (RHZE) for 2 months, followed by a two-drug regimen (RH) for 8 months (total duration of treatment being 10 months). The current formulations for treating TB children are child friendly and available as RHZ, 75/50/150 (fixed dose combination) and Ethambutol 100 as a single formulation i.e., RHZ + E for the intensive phase and RH, 75/50 (fixed dose combination) for the continuation phase.

### **iv. Other forms of EPTB (e.g., abdominal TB)** should be treated with a 6-month treatment regimen of 2RHZE/4RH.

- The use of fixed-dose combination (FDC) tablets is recommended over separate drug formulations in treatment of patients with drug-susceptible TB.
- Ethambutol is safe for use in children provided the recommended doses are adhered to

Table 33 Summary of the recommended TB treatment regimens for children diagnosed with drug susceptible TB

<b>Regimen</b>	<b>2RHZE/ 2RH</b>	<b>2RHZE/ 4RH</b>	<b>6RHZEthionamide</b>	<b>2RHZE/ 10RH</b>
Duration	(4 months)	(6 months)	(6 months)	(12 months)
Type of TB	PTB	PTB	TB meningitis	Bone TB
	TB adenitis	EPTB (Excluding TB meningitis and Bone TB)		TB meningitis
Eligibility	HIV negative children aged 3 months to 14 years	Children who are not eligible for the 4 months regimen	HIV negative children and adolescents aged 0 – 19 years	Children and adolescents aged 0 – 19 years with bone TB and TB meningitis
	WHO FULFILL ALL THE CRITERIA BELOW	All infants aged 0 - < 3 months		All HIV positive children and adolescents with TB meningitis
	Mild symptoms and does not require hospitalization	All adolescents aged ≥ 15 years		Children with TB meningitis who are not eligible for the short intensive 6 months (6RHZEthionamide) regimen
	No severe malnutrition	All HIV positive children and adolescents		
	Negative TB test result			
	No miliary TB pattern or cavitation or airway obstruction, or complicated pleural effusion on CXR (if available)			
	This includes those that meet the above criteria with peripheral TB adenitis			

### Management of children previously treated for TB

Retreated TB care depends on drug susceptibility (see Table 34 below).

Table 34 How to manage children previously treated for TB

<b>Category</b>	<b>What to do</b>	<b>Comments</b>
Children previously treated for TB (Re-treatment cases e.g., relapse, lost to follow up, treatment failure)	• Obtain a sample	• If Xpert/Truenat reveals TB and Rifampicin sensitivity treat as new patient under DOT
	• Do Xpert/Truenat to screen for Rifampicin resistance	• If Xpert/Truenat reveals TB and Rifampicin resistance, refer child to MDR treatment site
		• If Xpert/Truenat is negative, obtain another sample and send it to NTRL for culture. Refer the child to a higher-level facility for further evaluation
		• If unable to obtain a sample refer the child to a higher-level facility for further evaluation

Table 35 Dosing table for first-line medicines

<b>Medicine</b>	<b>Dose</b>	<b>Dose Range</b>
Isoniazid (H)	10 mg/kg	7–15 mg/kg
Rifampicin (R)	15 mg/kg	10–20 mg/kg
Pyrazinamide (Z)	35 mg/kg	30–40 mg/kg
Ethambutol (E)	20 mg/kg	15–25 mg/kg

*Table 36 Dosing table for first-line medicines using weight bands*

Weight (kg)	Number of tablets		
	Intensive phase RHZ 75/50/150 mg	E 100 mg	Continuation phase RH 75/50mg
4-<8	1	1	1
8-<12	2	2	2
12-<16	3	3	3
16-<25	4	4	4
≥25	Adult dosages recommended		

Children ≥25 kg should follow adult dosing guidelines using adult formulations (Table 37).

*Table 37 Dosing for children >25 kg using adult FDCs*

Weight band	RHZE	RH
	150/75/275/400 mg	150/75 mg
25 - <30	2	2
30 - <35	3	3
35 - <50	4	4
50 - <65	4	4
≥65	5	5

*Table 38 Dosage for the short intensive 6 months treatment for TB meningitis (6RHZEthionamide)*

Medicine	Dose (mg/kg body weight)
Isoniazid (H)	15 - 20
Rifampicin (R)	22.5 - 30
Pyrazinamide (Z)	35 - 45
Ethionamide (Eto)	17.5 – 22.5

*Table 39 Treatment interruption management for children with drug-susceptible TB.*

Treatment phase of interruption	Details of interruption	Management
<b>Intensive phase</b>		
Intensive Phase: applies to 4- and 6-month regimens	Interruption < 14 days	Continue treatment and complete all intensive phase doses
	Interruption ≥ 14 days	Restart intensive phase
<b>Continuation phase (4-month 2RHZE/2RH regimen)</b>		
Continuation phase (4-month regimen)	Completed ≥80% of doses (≥ 45 doses) within 8 weeks	Further treatment not necessary
Continuation phase (4-month regimen)	Completed <80% of doses (< 45 doses) and cumulative interruption <1 month	Complete remaining doses of treatment
Continuation phase (4-month regimen)	Completed <80% of doses (< 45 doses) and cumulative interruption >1 month	Restart treatment from beginning of intensive phase
<b>Continuation phase (6-month 2RHZE/4RH regimen)</b>		
Continuation phase (6-month regimen) and bacteriologically negative at initiation	Completed ≥80% of doses (≥ 90 doses) within 16 weeks	Further treatment not necessary
Continuation phase (6-month regimen) and bacteriologically positive at initiation	Completed ≥80% of doses (≥ 90 doses) within 16 weeks	Complete remaining doses of treatment If consecutive lapse is >2 months, use clinical judgement
Continuation phase (6-month regimen)	Completed <80% of doses (< 90 doses) and cumulative interruption <2 months	Complete remaining doses of treatment
Continuation phase (6-month regimen)	Completed <80% of doses (< 90 doses) and cumulative interruption ≥2 months	Restart treatment from beginning of intensive phase, particularly if interruption was consecutive

## **Adjunct therapy**

1. Pyridoxine: Prevents peripheral neuropathy, especially in children with severe malnutrition and children living with HIV. It is administered at a dosage of 0.5–1 mg/ kg/day. Prednisolone: Reduces severe inflammation and is indicated for TB meningitis, respiratory distress due to complications of airway obstruction by TB lymph nodes. Administer prednisolone at a dose is 2mg/kg/day as a single dose for 4 weeks, and then reduced over a period of 1- 2 weeks.
2. Nutritional support should be availed to children with malnutrition as per the national guidelines.

## **TB and comorbidities in children**

### **TB and malnutrition**

All children and adolescents initiated on TB treatment should undergo nutrition assessment and monitoring while on treatment. Details on the management of TB and malnutrition are listed in chapter 7.

### **TB and HIV**

All children diagnosed with TB and HIV should receive integrated care to facilitate retention and good outcomes. Details on the management of TB and HIV are listed in chapter 7.

## **Follow up and monitoring of children and adolescents on TB treatment**

Children and adolescents on TB treatment should be followed up at 2 and 4 weeks, at the end of the intensive phase (2 months), and monthly until treatment completion (4 or 6 months, depending on the regimen). Treatment outcomes are assessed at the end of treatment. For those living with HIV, TB follow-up should align with ART visits. Monitoring assessments should include:

- Assess for TB related symptom resolution or persistence, symptoms of side-effects of medicines, and other symptoms
- Measure weight. This is to ensure the right dose is administered at each visit/drug refill
- Assess adherence. This can be done by reviewing the treatment card and through discussions with the patient, caregivers and other treatment supporters
- Follow-up sputum smear microscopy for children with bacteriologically confirmed TB at 2 months after the start of treatment, 5 and 6 months. Stool is NOT a recommended sample for treatment monitoring. Symptomatic improvement and weight gain are, however, more valuable markers of treatment success or failure. If a follow-up smear is positive, the patient should complete additional investigations to assess for drug resistance (Xpert MTB/RIF Ultra, Truenat, TB culture and DST or molecular tests for drug resistance) and other causes of poor treatment response.
- Repeat sample collection at 2 months in children with clinically diagnosed TB is not indicated unless there is an inadequate clinical response without symptomatic and nutritional improvement.
- Follow-up CXR is not needed if the child is responding well to TB treatment. Children commonly have a slow radiographic response to treatment and may have persistent radiographic abnormalities at treatment completion, but this does not mean they are not responding to treatment.
- Models of care for child and adolescent TB may be facility or community based as described in section 4.2.1.3

## Indications for admission and or referral of children and adolescents on TB treatment

There are instances where children and adolescents need to be admitted or referred to other health facilities. The indications for referral or hospitalization of children and adolescents with Tuberculosis during TB treatment or evaluation include:

1. Severe forms of TB including TB meningitis, TB pericarditis, miliary TB with respiratory distress and TB spine with neurological complications
2. Severe malnutrition - for nutritional rehabilitation
3. Severe pneumonia (i.e., chest in-drawing)
4. Other co-morbidities e.g., severe anemia, liver disease, renal disease
5. Severe adverse reactions such as hepatotoxicity
6. Neonate weighing less than 4 kg
7. Advanced HIV Disease in a very sick child (with danger signs)

## TB contact investigation

TB contact investigation identifies undiagnosed TB or TB infection among contacts of a TB patient, including children and adolescents. It is crucial for prompt treatment initiation or identifying at-risk children and adolescents. The steps in contact investigation include:

- i. Review available information on the index patient
- ii. Assess the duration and degree of infectiousness of the index patient to identify contacts
- iii. Counsel the index patient and enumerate household and close contacts
- iv. Develop a plan for contact investigation in consultation with the index patient or their parent or guardian
- v. Consider other contacts for investigation
- vi. Conduct home visits or invite contacts to the health centre for screening for TB infection or TB disease
- vii. Conduct a clinical assessment of contacts and refer for testing for TB infection or TB disease, and for HIV testing as appropriate
- viii. Provide treatment for TB disease or TPT as per eligibility, and provide ongoing support until treatment completion
- ix. Review the completeness of the contact investigation and attempt to follow up on missing contacts and complete missing information
- x. Ensure systematic recording and reporting of the whole contact investigation process.

## Integration of TB into school health

It is important for the health worker to document whether a child or adolescent of school going age is attending school and conduct contact investigation within the school community as per the guidelines. This also provides an opportunity to increase awareness on TB. Learners with signs and symptoms of TB should be evaluated and those with TB initiated on treatment. Similarly, those without signs and symptoms should be assessed for TPT eligibility. Additionally, it is important to provide health education, treatment literacy, and psychosocial support to enhance adherence.

Most young children do not have infectious forms of TB. They can return to (pre) school as soon as they are feeling better and on treatment. Older children and adolescents, and younger children with positive bacteriological tests, should not attend school while they are infectious. After 2 weeks of starting TB treatment, if adherence is assured and there is clinical improvement, most children and adolescents are no longer infectious, can return to school, and do not need to wear masks for the purposes of preventing TB transmission.

In January 2023, the ministry of Education and Sports published a circular (Circular No. 01/2023) with recommendations on TB prevention in schools which should be implemented all schools. The recommendations include.

Learners are assessed for TB symptoms by a health worker before they report to school or at the beginning of each term. Those with TB symptoms should be linked to the nearest health facility for further assessment.

1. Learners on TB treatment should be attached to the school nurse or teacher in charge of health to ensure that they adhere to their TB medication and complete treatment.
2. Adequate ventilation and spacing both in the classrooms and the dormitories.
3. Integrate the Ministry of Health recommended TB messages into school activities such as edutainment, debates, talking compounds
4. School administration should ensure adherence to the recommended hygiene standards

## CHAPTER 8: TUBERCULOSIS AND COMORBIDITIES

TB comorbidities are concurrent health conditions that increase the risk of developing TB and poor treatment outcomes. Common comorbidities include diabetes, HIV, alcohol use, malnutrition, mental health disorders, and viral hepatitis.

These conditions can lead to treatment failure, death, or relapse. For example, people with TB and diabetes are twice as likely to die during treatment, and those with HIV are 20 times more likely to develop TB. These conditions can lead to treatment failure, death, or relapse. For example, people with TB and diabetes are twice as likely to die during treatment, and those with HIV are 20 times more likely to develop TB.

Addressing comorbidities is crucial for improving TB treatment outcomes and reducing socioeconomic impact.

An overview of strategies to manage TB comorbidities is represented in Table 40 below.

*Table 40 Interventions to address TB and comorbidities*

<b>Reduce the burden of TB among people with health-related risk factors</b>	<b>Reduce the burden of comorbidities among people with TB</b>
Prevent TB among people with identified health-related risk factors through health education, infection prevention and control as well as provision TB preventive therapy.	Prevent comorbidities among people with TB through SBCC interventions.
Find and treat TB among people with key health-related risk factors for TB disease, through screening or intensified case-finding, diagnosis and appropriate treatment.	Find and treat comorbidities among people with TB through screening, diagnosis and treatment of comorbidities associated with poor TB treatment outcomes

Table 41 below summarizes the WHO 2022 recommended interventions for the TB health-related risk factors and comorbidities.

*Table 41 Health-related risk factors and TB comorbidities with related interventions*

<b>Health-related risk factors for TB</b>	<b>Interventions to reduce the burden of TB among people with comorbidities and health-related risk factors</b>				
Key drivers for TB /associated with poor TB treatment outcomes	Find and treat TB	TB Preventive Therapy	Infection Prevention and Control (IPC)	Counsel on and prevent comorbidities	
Diabetes	✓	□	✓	✓	
Disorders due to alcohol use	✓	□	✓	✓	
HIV	✓	✓	✓	✓	
Smoking	✓	□	✓	✓	
Undernutrition	✓	□	✓	✓	

✓ recommendation exists; □ Currently no recommendation exists

## TB-HIV Co-infection

HIV is the strongest risk factor for TB, with PLHIV up to 20 times more likely to develop TB due to weakened immunity. Uganda, a high TB/HIV burden country, has a 35.8% co-infection rate (2023-2024 NTLP report). TB is the leading cause of HIV-related hospitalization and death. TB/HIV treatment success is 86.7% compared to 89.4% overall, with a target of 93%. TPT coverage among PLHIV improved from 79% to 99%, with 98% completing therapy, and 99% of TB patients have documented HIV status. The NTLP and AIDS Control Program collaborate on TB/HIV activities, integrating HIV services to improve outcomes.

*Table 42 TB / HIV collaborative activities*

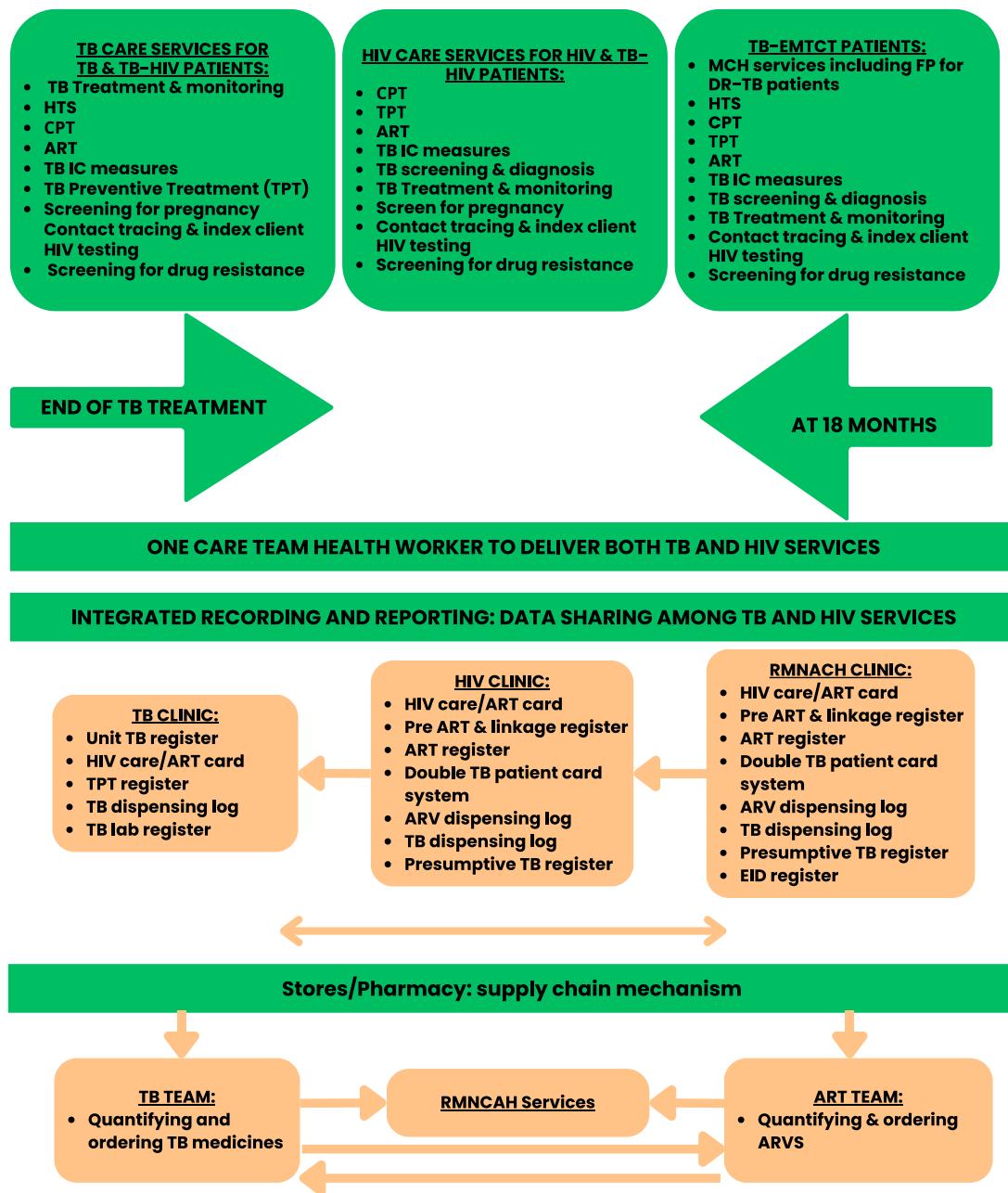
<b>Strengthen the mechanisms for collaboration between TB and HIV control programs for delivering integrated TB and HIV services</b>
Strengthen coordinating mechanisms for TB and HIV collaborative activities at all levels.
Determine TB prevalence among people living with HIV (PLHIV) and HIV prevalence among patients with presumed and diagnosed TB
Carry out joint TB/HIV planning to integrate the delivery of TB and HIV services
Monitor and Evaluate collaborative TB/HIV activities
<b>Decrease burden of tuberculosis among people living with HIV and initiate early ART</b>
Intensify TB case finding and ensure high quality anti-TB treatment
Prevent TB through timely TB preventive therapy and ART initiation
Implement TB infection control practices in health care and congregate settings
<b>Decrease the burden of HIV among patients with presumptive &amp; diagnosed TB</b>
Provide HIV testing and counselling to clients presumed and diagnosed with TB
Provide HIV prevention interventions for clients presumed and diagnosed with TB
Provide Co-trimoxazole preventive therapy for TB patients living with HIV
Provide HIV prevention interventions, treatment care and support for patients with TB
Provide antiretroviral therapy to all patients co-infected with TB/HIV

Adapted from National collaborative guidelines on TB/HIV and other comorbidities version; 2024.

Adapted from National collaborative guidelines on TB/HIV and other comorbidities version; 2024.

The Uganda Ministry of Health recommends that TB and HIV services are provided at a single facility at the same time and location (one-stop shop service). A patient receives all the services they require at one care point on every visit. It includes the TB clinic providing HIV services and the HIV clinic providing TB services.

*Figure 20 One stop shop model for TB/HIV service delivery*



## **TB / HIV continuum of care**

The TB /HIV continuum of care consists of Systematic screening and diagnosis for TB, TB/HIV prevention and infection control, TB/HIV treatment, TB/HIV care and support.

### **Systematic screening and diagnosis for TB among People living with HIV**

All people living with HIV (children, adolescents & adults) should be screened with the WHO four-symptom screen (W4SS) at every encounter with a health-care worker, both to detect prevalent TB disease and to rule it out before initiation of TPT. The W4SS is likely to miss half of PLHIV with TB (may have accuracy related issues in certain populations and thus additional screening strategies e.g., CRP and/ or Chest X-ray are recommended). The different subpopulations and the recommended strategies for TB screening include.

#### **Screening for TB among PLHIV**

In all PLHIV, the W4SS and CRP or CXR (where available) shall be used to screen for TB. A presumed TB PLHIV case will either have a positive symptom screen, a CRP result of  $>5\text{mg/l}$ , or an abnormal finding on CXR.

#### **Diagnosis of TB in PLHIV**

PLHIV without advanced HIV disease, who are presumed to have TB, diagnosis using a mWRD test e.g., GeneXpert should be prioritized. For facilities without an mWRD on site, TB microscopy can be used to diagnose TB but a sample must be sent for GeneXpert testing at the nearest facility for rifampicin resistance testing.

**People with Advanced HIV Disease (AHD)** (i.e. $\text{CD4} \leq 200 \text{ cells}/\mu\text{l}$  or in clinical stage 3 or 4), TB diagnosis using LF-LAM, supplemented with mWRD e.g., GeneXpert is recommended.

**PLHIV with a non-suppressed viral load,** shall be assessed for AHD and then follow the guidelines described above.

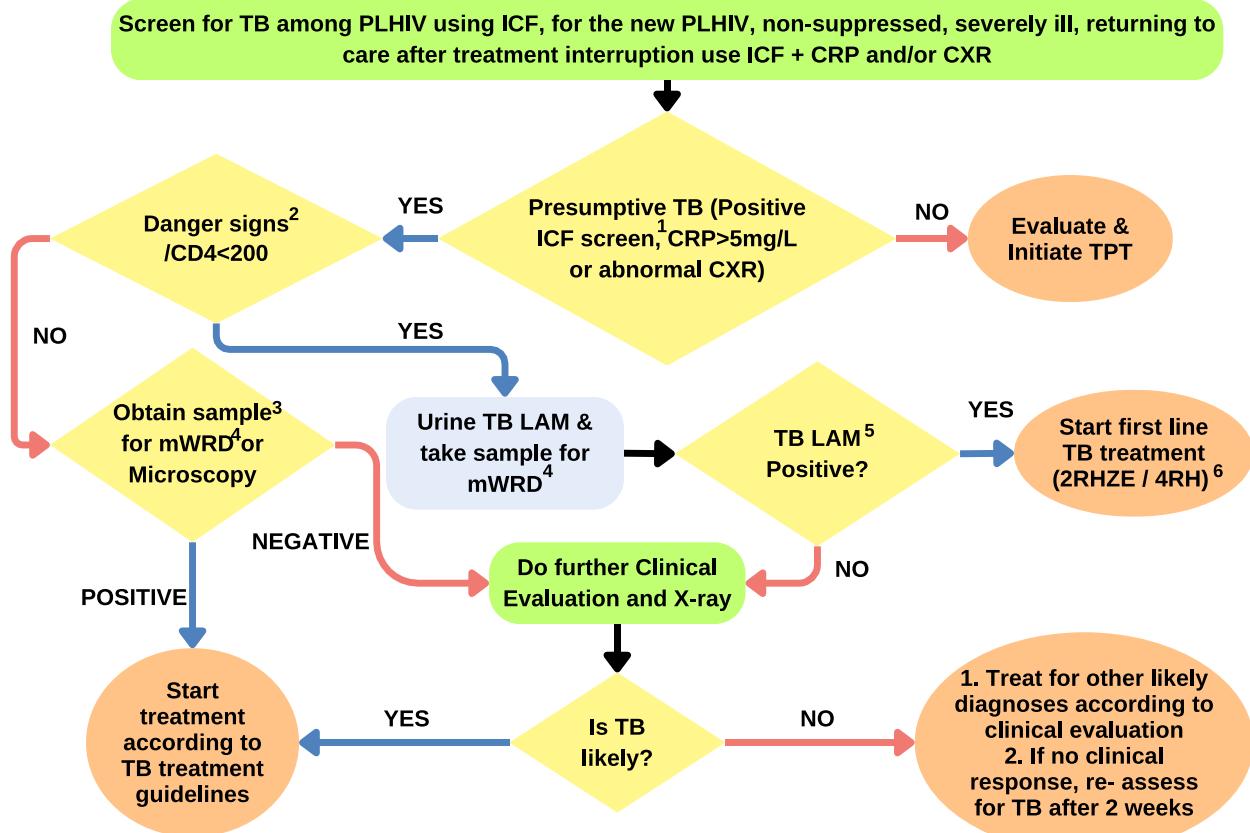
All **inpatient PLHIV** shall be assessed for AHD and TB at any episode of hospitalization regardless of their ART status

Pregnant women living with HIV: TB screening for this population should be integrated with prevention of mother-to-child transmission and antenatal care

Figure 21 Algorithm for screening, diagnosis and management of TB among PLHIV



## ALGORITHM FOR SCREENING, DIAGNOSIS AND MANAGEMENT OF TB AMONG PEOPLE LIVING WITH HIV



1. Positive ICF screen is presence of current cough, fever > 2-week, noticeable weight loss, excessive night sweats, if child- poor weight gain and history of contact with a PTB patient

2. Danger signs for adults refer to signs of a seriously sick person and they include respiratory rate > 30/min, temperature >39 °C, heart rate 120/min and unable to walk unaided. Danger signs for children include lethargy, convulsions, inability to feed, repeated vomiting, temperature above 39°C and tachycardia/tachypnea.

3. Appropriate sample types include; sputum, CSF, Gastric aspirate, urine, stool

4. Do a Molecular WHO Recommended Diagnostic (mWRD) test e.g., Genexpert, TRUNAAT, if you are able to obtain a specimen, so as to rule out rifampicin resistance. Note TB LAMP does not detect rifampicin resistance.

5. For any TB LAM positive other Co-morbidities such as Cryptococcus, bacterial infections should be ruled out.

6. Refer to higher centers for TB treatment if it is unavailable or if MDR-TB is diagnosed or incase of toxicity while on TB treatment

Note: Children less than 5 years who are new and have been on ART for less than one year are eligible for a TB LAM test if they have AHD symptoms and signs (refer to the symptom screen and advanced disease management pathway).

## **TB Preventive Treatment (TPT) among PLHIV**

When PLHIV have any one of the four symptoms (current cough, fever, weight loss or night sweats), they may have active TB and should be evaluated for TB and other diseases prior to TPT initiation. TPT initiation should only be undertaken after active TB disease has been ruled out.

Adults and adolescents living with HIV who are unlikely to have active TB should receive TPT as part of a comprehensive package of HIV care. The combined use of TPT and ART among PLHIV significantly reduces the incidence of TB. TPT should be given to; those on ART, pregnant women and those who have previously been treated for TB, irrespective of the degree of immunosuppression.

TPT reduces the overall risk for TB by 33% among PLHIV, with the reduction increasing in those who are TST positive. However, TPT should still be given even if testing for latent TB infection is not available.

The following regimens could be used for TPT as guided in Table 43 and Table 44 below:

- 6H: Daily Isoniazid for 6 months.

Note: Isoniazid may be available in combination with co-trimoxazole and pyridoxine as a fixed dose combination referred to as Q-TIB: In this case, Q-TIB is also administered daily for 6 months.

- 3HP: Weekly Isoniazid and Rifapentine for 3 months (recommended for patients aged more than 2 years).
- 3HR: Daily Rifampicin and Isoniazid for 3 months (recommended for children less than 15 years).

NOTE: TPT regimen containing Isoniazid should be used together with pyridoxine to prevent peripheral neuropathy

## **Eligibility for TPT**

- Infants aged <one year living with HIV who are in contact with a person with TB and who are unlikely to have active TB on an appropriate clinical evaluation or according to national guidelines should receive TB preventive treatment
- HIV-positive children ( $\geq$ one year of age), adolescents and adults with no signs and symptoms of TB irrespective of ART status
- HIV-positive infants and children <5 years with a history of TB contact who have no signs and symptoms of active TB disease, irrespective of previous TPT.
- HIV-positive pregnant mothers with a history of contact with a TB patient after ruling out active TB.
- HIV-positive pregnant mothers with a WHO Stage 3 or 4 event and/or CD4<200 without active TB.
- TPT should also be given to those who have previously been treated for TB immediately after completing TB treatment.

Note: TPT should be offered to eligible patients irrespective of the degree of immunosuppression and even when latent TB infection testing is unavailable.

- For HIV-positive pregnant mothers without a history of TB exposure, TPT will be deferred until 3 months after delivery.
- For HIV positive women and adolescent girls on TPT who get pregnant, continue and complete the TPT while closely monitoring for side effects.

Table 43 TPT regimens for adolescents ≥ 15 years and adults on ART

ARV Drug Regimen	TPT regimen Options	Rationale for TPT regimen
TDF or AZT or ABC + 3TC + DTG	Isoniazid (6H) or Isoniazid-Rifapentine- based regimens	No dose adjustment of DTG with Isoniazid-Rifapentine-based regimen
TDF or AZT or ABC + 3TC+ ATV/r	Isoniazid (6H)	Co-administration of rifamycins (such as rifampicin) with protease inhibitors has been associated with reduction in plasma levels of protease inhibitors.
TDF or AZT or ABC + 3TC + LPV/r		
TDF or AZT or ABC + 3TC+EFV	Isoniazid (6H) Isoniazid (6H) or Isoniazid-Rifapentine- based regimens	A higher dose of EFV, i.e., 600mg is recommended if Isoniazid/Rifapentine-based regimen is used

Table 44 TPT regimen for children < 15 years on ART

ARV Regimen	TPT regimen options	Rationale for TPT regimen
ABC or AZT +3TC+LPV/r	Isoniazid (6H)	Co-administration of rifamycins (such as rifampicin) with protease inhibitors has been associated with reduction in plasma levels of protease inhibitors.
ABC or AZT+3TC +ATV/r		
ABC or AZT+ 3TC+DTG	Isoniazid (6H) or Rifampicin/ Isoniazid (3RH or Isoniazid/Rifapentine- based regimens (for children aged > 2 years)	Double the dose of DTG if 3RH is used (Awaiting feedback following consultation on double DTG dosing for children <18yrs to be harmonised in the circular).
ABC or AZT +3TC+ EFV		Lack of data to support the use of Rifapentine among children aged < 2 years.
ABC or AZT + 3TC+RAL		Double the dose of RAL if 3RH is used
		Lack of data to support the use of Rifapentine among children aged < 2 years.

### Co-administration of DTG and TPT

Though DTG and INH are well-tolerated together, both can cause liver injury. Recommendations for co-administration are as follows.

- New Patient:** For newly identified patients, start on Tenofovir, Lamivudine and Dolutegravir (TLD) with active symptomatic monitoring for adverse events. Initiate TPT after 3 months to allow time for potential unmasking of TB and to monitor any toxicities that may arise from DTG, prior to initiation of TPT.
- For stable patients already transitioned to DTG:** If patient has been on TLD for 3 months or more, initiate TPT immediately.
- If client is already on TPT and on a non-DTG based regimen:** Optimization to DTG will be deferred until completion of TPT.
- Stable patients for DTG transition and have not received TPT before:**
  - In case TLE stock is available: First complete TPT and then transition to DTG.
  - In case TLE stock is not available: Transition to DTG and initiate TPT after 3 months.

Note: All patients receiving INH prophylaxis and DTG+INH should be closely monitored for signs and symptoms of liver toxicity as specified in the pharmacovigilance guidelines.

## **Infection Control**

PLHIV face high TB risk in healthcare and congregate settings, requiring infection control measures. Facilities should have a TB IC committee, plan (managerial, administrative, environmental, and personal protection), and a focal person (see Chapter 8).

## **HIV/AIDS care and support in TB clinics**

The provision of HIV/AIDS care in TB clinics is part of a continuum of a comprehensive AIDS care package. The package includes clinical management and laboratory support (prophylaxis, early diagnosis of TB or HIV/AIDS, rational treatment and follow-up care for non-TB opportunistic infections). Those who have completed their TB treatment should continue with HIV care service or be referred where such a service can be offered.

TB/HIV collaborative care aims to provide comprehensive care to the TB/HIV co-infected patient. As part of TB/HIV collaborative activities, the following should be planned and carried out in TB clinics:

### **i. Provider Initiated HIV testing and counselling**

HIV testing of patients with presumptive and diagnosed TB should be provider initiated. Provider- initiated testing and counselling (PITC) is HIV testing and counselling offered by a health-care provider in a clinical setting. PITC is recommended to everyone (all adults and children) with presumptive and diagnosed TB. Provider-initiated testing and counselling should be voluntary and should be provided according to the national HIV counselling guidelines.

### **ii. HIV prevention methods in the TB clinics**

Health workers should provide; HIV prevention messages, PrEP, PEP. Positive living among those already infected and safe sex practices, including provision and correct use of condoms should be emphasized in order to prevent spread within the community. All clients attending the TB clinics should be screened for sexually transmitted diseases (STDs) using the recommended approaches. Those with symptoms of sexually transmitted infections should be treated or referred to an STD clinic. A referral linkage should be established within and between TB and HIV service provision points.

### **iii. Co-trimoxazole preventive therapy (CPT)**

Routine Co-trimoxazole preventive therapy should be administered to all HIV-infected patients (including children and pregnant women) with active TB disease regardless of CD4 cell count. Co- trimoxazole preventive therapy should be implemented as an integral component of the TB-HIV care package because it is effective in reducing new WHO stage 3 or 4 clinical events, severe bacterial infections, malaria and hospitalization.

### **iv. Provision of antiretroviral treatment**

All TB patients co-infected with HIV should be given antiretroviral drugs. Antiretroviral therapy should be started If the drugs cannot be obtained at the facility, the patient should be referred to a facility where they can obtain the drugs.

## **Community Involvement in TB/HIV activities**

Through support groups for people living with HIV/AIDS, Peer-to-Peer support groups, village health teams (VHTs) and community-based organizations, TB prevention and care should be integrated with HIV/AIDS prevention, care and support. Communities should be effectively mobilized to advocate for resources and opportunities to implement collaborative TB/HIV activities. Community-based organizations, CB-DOTS treatment supporters and workplace managers or staff associations should also be involved in identifying people with symptoms and signs of TB or HIV/AIDS, referring them to health facilities for diagnosis and treatment and ensuring directly observed treatment. Innovative mechanisms for delivery of ART could be designed along these same lines.

## **Monitoring and Evaluation of Collaborative TB/HIV Activities**

Monitoring and evaluation provide the means to assess the quality, effectiveness, coverage and delivery of collaborative TB/HIV activities. It ensures continuous improvement aimed at improving individual and joint programme performance. Monitoring and evaluation involve collection and analysis of data for indicators of TB/HIV collaborative activities. These data are collected from the level of provision of service centred into the Uganda National Q.I Database based on which it is routinely

## **Presentation of TB in HIV infected persons**

The clinical presentation of TB in early HIV infection is similar to that in HIV-negative persons.

However, as HIV infection progresses, CD4+ T lymphocytes will decline in number and function. These cells play an important role in the body's defence against tubercle bacilli. Thus, the immune system becomes less able to prevent growth and local spread of *Mycobacterium tuberculosis*. Disseminated and extra pulmonary TB diseases become more common.

Extra pulmonary TB (EPTB) and clinically diagnosed TB are more common among HIV positive than HIV negative persons. Furthermore, the more advanced the immunosuppression, the more TB tends towards clinically diagnosed, EPTB and disseminated forms.

## **Pulmonary TB in HIV-infected patients**

Even in HIV-infected patients, PTB is still the commonest form of TB. The presentation depends on the severity of immunosuppression. Table 42 below shows how the clinical picture, sputum result and chest X-ray appearance often differ in early and late HIV infection.

*Table 45 Comparison of pulmonary TB in early and late HIV infection among adolescents and adults*

Features of PTB	Stage of HIV infection	
	Early	Late
Clinical picture	Often resembles post-primary PTB	Often resembles primary PTB
Sputum smear result	Often positive	Often negative
Chest X-ray appearance	Often cavities	Often infiltrates with no cavities

### **Extra pulmonary TB in HIV-infected patients**

The usual forms of extra pulmonary TB: Pleural TB, lymph node, TB Pericarditis, miliary TB, TB meningitis, Abdominal TB, TB Bone and joint and disseminated TB (with myco-bacteraemia) can occur in patients who are HIV positive. Occurrence of extra pulmonary TB (except TB lymph node only) implies severe HIV disease (WHO disease classification stage 4).

### **Diagnosis of TB in HIV-Infected Patients**

Diagnosis of TB among people infected with HIV follows the same principles as in HIV negative individuals. There are however some differences that must be noted. HIV infected persons tend to have smear negative TB, they have atypical radiological presentations of TB and they present more with disseminated TB. There are newer tests that have better accuracy in HIV infected persons such as the WHO recommended molecular diagnostics e.g. Xpert MTB Ultra. The NTLP TB diagnostic algorithm recommends that these tests are used as the first tests to diagnose TB among HIV infected persons. Other tests have also been developed to support the diagnosis of TB and can be used based on the level of immunosuppression. One such test is the TB-LAM which can be used in HIV positive patients with severe immunosuppression.

### **TB Treatment in HIV-Infected Patients**

All patients diagnosed with TB, including those who are HIV infected should be treated with anti-TB drugs according to the NTLP recommendations. All patients on TB treatment should be supported to adhere and complete their medications. Antiretroviral therapy should be offered to all HIV-positive TB patients, according to the national ART and care guidelines for all adults and children.

### **Considerations for ART initiation in TB/HIV co-infection**

#### **Timing of ART for adults, adolescents and children being treated for HIV-associated TB**

ART should be started as soon as possible, two weeks after initiating TB treatment, regardless of CD4 cell count, among people living with HIV (except when signs and symptoms of meningitis are present).

- i. If the patient is already on ART, start TB treatment immediately and adjust the ART regimen as recommended below (Table 43).
- ii. If the patient is not on ART, initiate anti-TB treatment immediately and start ART two weeks after initiation of TB treatment. ART should be initiated two weeks after starting anti-TB treatment.
- iii. If the patient is not on ART and is diagnosed with MDR-TB, ART should be initiated 4-6 weeks after second-line TB treatment initiation. However, if the patient is already on ART, continue ART and adjust ART regimen as per the MDR TB guidelines.

## Common TB-ART Treatment Regimens

A trained staff or medical officer needs to decide when to start ART and the ART regimen to be initiated on. For patients being considered for, or already on TB-ART co-treatment, the attending health worker should note the following:

A patient on TB-ART co-treatment will have many tablets to swallow and may experience more side-effects. The patient should be educated on how to manage mild to moderate side-effects and report to the health worker immediately for severe ones. The patient continues receiving Cotrimoxazole. There are many tablets and several changes may take place in the regimen during the course of treatment. This requires careful education of the patient and treatment supporter at each change. The TB treatment is not necessarily in the morning.

The following examples are based on a Rifampicin-based regimen during the initial and continuation phases of TB treatment. The patient is put on an Efavirenz-based ART regimen if it is started during TB treatment.

*Table 46 Recommended first line antiretroviral therapy regimens for adult patients on anti-TB treatment*

Patient category	Recommended ART regimens	Alternative ART regimens
<b>Adults and adolescents ≥30Kg, including pregnant &amp; breastfeeding women</b>	TDF+3TC+DTG or TAF+FTC+DTG Increase dose of DTG to twice a day	If TDF or TAF is contraindicated, use ABC:  ABC or TAF+FTC+DTG; Increase dose of DTG to twice a day  If DTG is contraindicated, use EFV:  TDF or ABC → +3TC+ EFV400 <b>OR</b> TAF+FTC+EFV400  No dose adjustments  If DTG and EFV are contraindicated, use ATV/r:  TDF or ABC → +3TC+ATV/r or  TAF+FTC+ATV  Substitute Rifampicin with Rifabutin
<b>Children ≥20Kg - &lt;30Kg</b>	ABC +3TC+ DTG or TAF+FTC+DTG Increase dose of DTG to twice a day	If ABC is contraindicated, use AZT or TAF:  ABC +3TC+ DTG <b>OR</b> TAF+FTC+DTG  Increase dose of DTG to twice a day  If DTG is contraindicated, use LPV/r or EFV:  ABC or AZT +3TC+LPV/r <b>OR</b> TAF+FTC+LPV/r  Double both the morning and evening doses of LPV/r. After TB treatment return to normal dose of LPV/r. <b>OR</b> Substitute Rifampicin with Rifabutin  <b>ABC or AZT+3TC+EFV or TAF+FTC+EFV</b>  <b>In children &gt;3 years - Substitute EFV with DTG or LPV/r after TB treatment</b>

EFV=efavirenz, NVP = Nevirapine, TDF=tenofovir, Zidovudine (AZT), 3TC= Lamivudine, FTC= Emtricitabine (FTC), DTG=Dolutegravir

## **ART regimen substitutions for patients diagnosed with TB while on ART**

Anti-TB treatment should be initiated immediately upon diagnosis while continuing ART. However, the ARV regimen should be reviewed and may need substitutions to ensure optimal treatment of both TB and HIV and to decrease the potential for toxicities and drug–drug interactions (Table 44). The following should be noted.

- i. In case ARVs are to be substituted in patients initiating TB treatment while on ART, careful consideration of previous ART regimens should be taken in order not to give an ARV to which the client may already have resistance.
- ii. Raltegravir (given as a double dose) is recommended in TB-HIV co-treatment for children who cannot tolerate double dosing of LPV/r or for whom Rifabutin is unavailable for treatment with DRV/r.
- iii. Children on NVP-based regimens should be switched to a triple NRTI regimen (ABC+3TC+AZT) only if EFV is contraindicated, as this is an inferior regimen.
- iv. After completion of TB treatment, ensure that the ART regimen is optimized:
  - If virally suppressed, optimize the regimen.
  - For adults, when optimizing 2nd line PI-based regimens, ensure that the client was not previously exposed to DTG in the 1st line ART regimen. If the client was on a DTG-based 1st line ART Regimen and is currently on a PI-based 2nd line regimen and virally suppressed, maintain the PI-based regimen after TB treatment.

If viral load is not suppressed switch the client to 2nd or 3rd line

*Table 47 ARV regimen substitutions for patients initiating TB treatment while already on ART*

<b>Age Group</b>	<b>Regimen when diagnosed with TB</b>	<b>Recommended action/substitution</b>
Adults and adolescents ≥30Kg including pregnant and breastfeeding women	If on EFV-based regimen*	Continue with the same regimen and dose. After TB treatment optimize the regimen if virally suppressed (substitute EFV with DTG). If not virally suppressed switch to 2 <sup>nd</sup> line ART.
	If on DTG-based regimen	Continue the same regimen but increase the dose of DTG (give DTG 50mg twice daily instead of once daily). After TB treatment return to DTG once a day.
	If on NVP-based regimen*	Substitute NVP with EFV. After TB treatment optimize ART regimen if virally suppressed (substitute EFV with DTG). If not virally suppressed switch to 2 <sup>nd</sup> line ART.
	If on ATV/r-based regimen*	<p><sup>8</sup> Continue the same regimen but substitute Rifampicin with Rifabutin  <sup>OR</sup></p> <p><sup>9</sup> If on 2<sup>nd</sup> line, substitute ATV/r with LPV/r and double both the morning and evening doses of LPV/r. If virally suppressed after TB treatment, return to ATV/r (if there is previous exposure to DTG) or optimize to DTG-based regimen if no previous DTG exposure.  <sup>OR</sup></p> <p><sup>10</sup> If on 1<sup>st</sup> line and EFV is not contraindicated, substitute ATV/r with EFV for the duration of TB treatment. After TB treatment optimize the regimen if virally suppressed.</p> <p><sup>11</sup> If not virally suppressed after TB treatment, switch to 2<sup>nd</sup> line or 3<sup>rd</sup> line (with HIVDR).</p>
	If on LPV/r -based regimen*	<ul style="list-style-type: none"> <li>• Double both the morning and evening doses of LPV/r. If virally suppressed after TB treatment, return to normal dose of LPV/r (if on 2<sup>nd</sup> line with previous DTG-based regimen) or optimize to DTG-based regimen if no previous DTG exposure. After TB treatment return to normal dose of LPV/r.</li> <li>OR</li> <li><sup>12</sup> Substitute Rifampicin with Rifabutin</li> <li><sup>13</sup> If not virally suppressed after TB treatment, switch to 2<sup>nd</sup> line or 3<sup>rd</sup> line (with HIVDR).</li> </ul>

(Continued overleaf)

<b>Age Group</b>	<b>Regimen when diagnosed with TB</b>	<b>Recommended action/substitution</b>
Children ≥ 20Kg- <30Kg	If on DTG-based regimen	Continue the same regimen but increase the dose of DTG to twice daily. After TB treatment, return to DTG once a day.
	If on EFV-based regimen*	Continue the same regimen. After TB treatment optimize the regimen if virally suppressed (substitute EFV with DTG). If not virally suppressed switch to 2 <sup>nd</sup> line ART
	If on NVP -based regimen*	<ul style="list-style-type: none"> <li>• Substitute NVP with EFV (if &gt;3 years and &gt;10Kg)</li> <li>OR</li> <li>• If EFV is contraindicated, give a triple NRTI regimen (ABC+3TC+AZT).</li> </ul> <p>After TB treatment optimize treatment with a DTG-based regimen if virally suppressed. If not virally suppressed switch to 2<sup>nd</sup> line ART</p>
	If on LPV/r-based regimen	<p>Double both the morning and evening doses of LPV/r. After TB treatment return to normal dose of LPV/r.</p> <p>OR</p> <p>Substitute Rifampicin with Rifabutin.</p> <p><i>If the child cannot tolerate double dose of LPV/r</i></p> <p>a) Substitute LPV/r with Raltegravir. Double the dose of Raltegravir. Return to LPV/r after completion of TB treatment.</p>
	If on DRV//r-based regimen	Substitute Rifampicin with Rifabutin
Children <20Kg	If on DTG-based regimen	Continue the same regimen but <b>increase the dose of DTG to twice daily</b> . After TB treatment, return to DTG once a day.
	If on LPV/r- based regimen	<ul style="list-style-type: none"> <li>• Continue the same regimen but either</li> </ul> <p>Super-boosting LPV/r morning and evening doses with additional ritonavir (RTV) (to make LPV/r ratio of 1:1 instead of 4:1, i.e., equal doses of LPV and RTV) After TB treatment return to normal dose of LPV/r.</p> <p>OR</p> <p>Substitute Rifampicin with Rifabutin.</p> <p><i>If the child cannot tolerate double dose of LPV/r</i></p> <p>b) Substitute LPV/r with Raltegravir. Double the dose of Raltegravir. Return to LPV/r after completion of TB treatment.</p>
	If on NVP-based regimen*	<ul style="list-style-type: none"> <li>• If &gt;3 years and &gt;10Kg substitute NVP with EFV.</li> <li>• If EFV is contraindicated, give a triple NRTI regimen (ABC+3TC+AZT).</li> <li>• If &lt;3 years and &lt;10Kg give triple NRTI regimen (ABC+3TC+AZT).</li> </ul> <p>After TB treatment optimize treatment with a DTG or LPV/r -based regimen if virally suppressed. If not virally suppressed switch to 2<sup>nd</sup> line ART.</p>
	If on DRV/r-based regimen	Substitute Rifampicin with Rifabutin

## **Children and adolescents with TB and HIV**

Children and adolescents living with HIV have an increased risk of TB exposure, infection, progression to disease, and TB-related morbidity and mortality, and the risk is largely driven by the degree of immune suppression.

The approach to diagnosing TB in children and adolescents living with HIV is essentially the same as diagnosing TB in HIV-negative children. TB diagnosis in children and adolescents living with HIV is however more challenging than in HIV-negative children due to the following reasons:

- i. Clinical features consistent with PTB are common in children and adolescents living with HIV but may be caused by other diseases and therefore lack specificity for a diagnosis of TB.
- ii. Most children living with HIV have been infected via mother-to-child transmission. The peak age prevalence for HIV is under 5 years. This is also the age group in which it is most difficult to confirm the cause of acute or chronic lung disease, including TB.
- iii. TST is less sensitive in children and adolescents living with HIV. Induration of >5 mm is considered positive if the child is living with HIV
- iv. Children and adolescents living with HIV have a very high incidence of acute and chronic lung diseases other than TB.
- v. Children and adolescents living with HIV may have lung disease of more than one single cause (coinfection), which can mask response to therapy.
- vi. There is an overlap of radiographic findings in TB and other HIV-related lung diseases.

Once a diagnosis of TB is made, TB treatment should be initiated irrespective of Anti-retroviral Therapy (ART) status. In addition to TB treatment, all children who are co-infected with TB and HIV should receive the comprehensive HIV care package including Anti-Retroviral Therapy (ART) and Co-trimoxazole Preventive Therapy (CPT). In addition, it is important to schedule the TB and HIV clinic appointments on the same day to enhance adherence and minimize loss to follow up. A child on TB-ART co-treatment requires close monitoring for side effects of both anti-TB medicines and ART. The tables below summarize the ART regimen for children with TB/HIV co-infection

### **1. Treatment of TB in children and adolescents living with HIV**

Children who are living with HIV should be treated for TB with a four-medicine regimen (Isoniazid, Rifampicin, pyrazinamide and ethambutol) for 2 months followed by a two-medicine regimen (Isoniazid and Rifampicin) for 4 months or 2 months (for non-severe TB) at standard dosages given daily. Eligibility for the 4-month treatment regimen depends on the severity of disease and can be determined using CXR features or clinical criteria.

### **2. ART in adolescents diagnosed with TB**

ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 count, among adolescents and children living with HIV (except when signs and symptoms of meningitis are present). Antiretroviral therapy should be delayed at least 4 weeks (and initiated within 8 weeks) after treatment for TB meningitis is initiated. The recommendation on the use of adjuvant corticosteroid therapy with dexamethasone or prednisolone (tapered over 6–8 weeks) also applies to children and adolescents living with HIV with TBM. The preferred ART regimen for children and adolescents on TB treatment are indicated in Table 47 above.

## **TB Immune Reconstitution Inflammatory Syndrome**

Immune Reconstitution Inflammatory Syndrome (IRIS) is also known as a paradoxical reaction and is an inflammatory process characterized by transient worsening of clinical disease following initiation of treatment due to restoration of the body's immunity, normally occurring within 3 months but mostly within the first month.

Risk factors for TB IRIS include; low baseline CD4 count, extensive TB disease, early initiation of ART, and rapid immunological and virological responses to ART.

There are two main presentations of TB-IRIS:

- i. Exacerbation of known TB disease in a child or adolescent living with HIV on TB treatment who is starting ART (paradoxical TB-IRIS)
- ii. Development of TB disease in a child or adolescent living with HIV starting ART (unmasking TB-IRIS).

Symptoms of TB IRIS include worsening TB symptoms and CXR features, new and persistent fevers after starting ART, and evidence of local and/or systemic infection or inflammation (e.g., enlarging lymph nodes and the development of fistulae and cold abscesses).

### **When IRIS is detected; the following actions should be taken:**

Rule out TB/HIV treatment failure, side effects of TB and HIV treatment, and pre-existing untreated opportunistic infections.

- Continue both ART and anti-TB treatment unless severe toxicity is suspected or confirmed (e.g., elevated LFTs). Give prednisolone at a dose of 1-2mg/kg for 1 to 2 weeks; and thereafter, gradually decrease the dose.
- Provide other supportive measures as needed.

## TUBERCULOSIS AND MALNUTRITION

### Introduction

Undernutrition is common among people with TB and increases the risk of progression to active disease, death, and relapse. Wasting in TB patients results from reduced appetite, altered metabolism, and inflammation. TB significantly impacts nutritional status, causing severe weight loss, altered protein metabolism, micronutrient deficiencies (e.g., vitamins A, D, E, C, Zinc, Selenium), and anaemia.

Good nutrition improves quality of life and aids recovery. This manual provides protocols for managing acute undernutrition, supporting health staff in delivering effective outpatient and inpatient care to improve patient outcomes.

*Table 48 Components of nutritional support*

Nutritional support within TB programs
a) Nutritional status assessment b) Risk factor and dietary assessment in malnourished TB patients c) Nutrition education and counselling on symptom-management and improved dietary intake during and after TB treatment and microbial cure d) Adequate diet for the management of TB infection and TB disease e) Targeted micronutrient supplementation (e.g., vitamin B6) f) Food support for management of undernutrition in TB patients g) Promotion of individual and household food security h) Management of moderate undernutrition i) Management of severe acute malnutrition j) Outpatient follow-up

### Nutritional status assessment

A good number of TB patients are undernourished at the time of diagnosis, and a nutrition assessment is key for an appropriate nutrition intervention and care. Due to the clear bidirectional causal link between undernutrition and active TB, nutrition screening, assessment and management are integral components of TB treatment and care.

The nutrition assessment can consist of anthropometric, biochemical, clinical measurements and dietary evaluation. The results from screening and assessment inform counselling, which is usually done at the time of diagnosis and throughout treatment.

### Nutrition screening of TB patients

- i. Take the weight and height of all patients except in pregnant women on the first visit
- ii. Calculate the Body Mass Index (BMI)
- iii.  $BMI = \text{Weight in kgs} / (\text{height in meters})^2$

Determine the nutritional status of the adult male, non-pregnant women as follows:

*Table 49 Nutritional status according to BMI*

Classification	BMI (kg/m <sup>2</sup> ) Principal cut-off points
Severe underweight	<16
Underweight	<18.5
Normal	18.5-<25
Overweight	25-<30
Obese	>30

- For children 5–18 years, use BMI-for-age charts; for those <5, use weight-for-height growth charts from MoH.
- Use Mid Upper Arm Circumference (MUAC) for assessing nutrition in pregnant women and individuals unable to measure weight and height (e.g., elderly with kyphosis).

### **Risk factor and dietary assessment in malnourished TB patients**

- Perform clinical assessment for other non-dietary causes of malnutrition, including identification of important comorbidities like HIV, diabetes mellitus or alcohol or drug abuse
- Perform biochemical assessment where possible
- Do dietary assessment, including assessment of individual and household food security.

### **Nutrition Education and Counselling for TB Patients**

- Focus on symptom management and improved dietary intake during and after TB treatment for recovery and microbial cure.
- Tailor counselling to address specific nutritional needs, including comorbid conditions like diabetes or HIV.
- Ensure nutrition education and counselling are delivered by a qualified nutritionist.

### **Optimal Diet for Managing TB Infection and Disease**

- A well-balanced and adequate diet are key to maintaining optimal health and physical function at all ages. Nutritional status is an important determinant of resistance to infection and of general well-being.
- The diet of a TB patient should include foods rich energy, protein, vitamin B6, vitamin A, zinc, iron and Vitamin D among others. Optimal intake of these nutrients may have a role in an individual's defence against TB.

### **Targeted micronutrient supplementation (e.g., vitamin B6)**

- A multivitamin and mineral supplement (50%-150% RDA) is recommended due to poor appetite and increased nutrient needs.
- TB patients on isoniazid should receive Vitamin B6 supplementation.
- Provide daily micronutrient supplements if fortified or supplementary foods are unavailable.
- Pregnant women with TB should receive multiple micronutrient supplements, including iron and folic acid, per UN guidelines.
- Calcium supplementation is recommended for pregnant women with TB in low-calcium settings to prevent pre-eclampsia.
- Lactating women with TB should receive multiple micronutrient supplements to meet maternal nutrient needs.

## **Food support for treatment of undernutrition in TB patients**

- Available supplementary food items can be used as supplementary food for severe and moderate undernutrition of TB patients.
- All patients who are not responding after three months should be reviewed by a respiratory physician along with a nutrition specialist.

*Table 50 Nutrients and common food sources*

Nutrients of focus	Food sources
<b>Protein</b>	Beans, Soya, meat, fish, chicken, eggs among others
<b>Carbohydrates</b>	Starchy staples, cereals and roots (maize, millet, sorghum, cassava, potatoes, yams, matooke)
<b>Zinc</b>	Fortified cereals, eggs, meat, fish among others
<b>Iron</b>	Meat, fish, poultry, organ meats, fortified grains, nuts, seeds, legumes, and vegetable among others
<b>Selenium</b>	Cereals, poultry, red meat, eggs
<b>Vitamins (A, E, D, B6)</b>	Fruits and vegetables (Carrots, tomatoes, strawberries, papaya, peaches, squash and pineapple, mangoes, pumpkin, orange flesh sweet potatoes, citrus fruits, avocado etc)

## **Promotion of individual and household food security**

- The health sector should address malnutrition and food insecurity, which hinder TB treatment access and adherence.
- Food security interventions can improve TB treatment adherence and support nutritional recovery.
- TB programmes can collaborate with food security and social protection services to ensure patients and families access adequate food and benefits.

## **Management of severe acute malnutrition**

Treat individuals with active TB and severe acute malnutrition, including children under 5, school-age children, adolescents, adults, and pregnant or lactating women, according to WHO guidelines specific to their age and condition.

## **Managing Moderate Undernutrition in TB Patients**

- **School-age Children, Adolescents, and Adults:** Evaluate those with persistent low BMI or weight loss during TB treatment for adherence and comorbidities. Provide nutrition counselling and fortified foods as needed.
- **Children Under 5:** Manage as per standard guidelines for moderate undernutrition, including nutrient-rich or fortified foods to restore proper weight-for-height.
- **Pregnant Women:** Provide nutrient-rich or fortified foods to support a weekly weight gain of ~300 g in the 2nd and 3rd trimesters.
- **MDR-TB Patients:** Supply fortified foods to restore normal nutritional status.

## **Outpatient Follow-Up**

- Conduct monthly follow-ups; for severe undernutrition, follow up fortnightly.
- Track weight gain to monitor progress.
- Coordinate follow-ups with other clinic visits.
- Reassess patients not gaining weight within 2–4 weeks.
- Refer patients with no improvement after three months to a respiratory physician and nutrition specialist.

## TUBERCULOSIS AND MENTAL HEALTH

People with TB are at higher risk for mental health issues, such as depression, which can negatively impact treatment outcomes. TB and mental health have a bidirectional relationship: TB can cause mental health issues due to stigma and reduced ability to work, while mental illness can increase TB risk through immune system effects. Up to 70% of TB patients experience mental illness, which can also interfere with TB treatment, as medications like linezolid and isoniazid interact, and TB drugs can reduce the effectiveness of antipsychotics. Mental health conditions like depression and anxiety can lead to poor treatment adherence, further worsening TB outcomes.

### A collaborative care framework for tuberculosis and mental health

Pillar 1 of the Global TB Programme's End TB Strategy emphasizes integrated, patient-centred care that includes managing co-morbidities like mental illness, which impacts TB treatment outcomes. Addressing mental health concerns through collaborative care improves patient well-being and treatment success.

Economic studies show that investing in mental health and TB care yields significant returns, reinforcing the need for integration. This can be achieved through a collaborative care model, involving a multidisciplinary team with mental health professionals and primary health care providers.

Key components of the collaborative care model:

- **Multi-professional Approach:** Involves a primary care provider and at least one other health professional (e.g., nurse, psychologist, psychiatrist).
- **Structured Management Plan:** Incorporates evidence-based guidelines, pharmacological (e.g., antidepressants) and non-pharmacological (e.g., CBT) interventions.
- **Scheduled Follow-ups:** Regular follow-ups to monitor symptoms, treatment adherence, and side effects.
- **Enhanced Communication:** Facilitates communication through meetings, case conferences, shared records, and feedback among care providers.

### Mental Health Care Package for TB Patients

1. **Training and Supervision:** Provide pre-service and in-service training on mental health, including basic knowledge, TB-related mental health, and counselling skills. Training should align with the **7 elements of mhGAP**:
  - i. Create awareness and understanding
  - ii. Provide mhGAP-IG training for educational leaders
  - iii. Assemble a team and make an action plan
  - iv. Review and adapt current curriculum
  - v. Deliver a pilot curriculum
  - vi. Evaluate and revise the curriculum
  - vii. Ensure ongoing supervision and mentorship for non-specialist workers.

2. **Screening for Mental Health Issues:** Use validated tools to screen for mental health disorders:
3. **GAD-7:** A 7-item, 21-point tool to assess anxiety levels over the past 2 weeks. Scores range from 0 (minimal) to 21 (severe) to gauge symptom severity.
4. **AUDIT:** A 40-point test to assess alcohol use, with scores indicating appropriate interventions from simple advice to diagnostic evaluation. **AUDIT-C** is a 3-question version to screen for hazardous drinking.
5. **Evidence-Based Interventions:** Apply mhGAP techniques for managing mental health issues, including cognitive behavioural therapy (CBT), behavioral action (BA), interpersonal therapy (IPT) for depression, and contingency management therapy (CMT), family counselling or therapy (FCT), motivational enhancement therapy (MET) for alcohol use disorders.
6. **Monitoring and Evaluation:** Implement M&E tools to track changes in mental health using screening results and assess the impact on TB treatment outcomes.
7. **Collaborative Care and Research:** Support integrated care for TB and mental health, and continue research to refine interventions and improve understanding of their relationship.

*Figure 22 Mental health screening tools for TB patients*

### Mental Health Screening Tools for TB Patients



**1. GAD-7 (Generalized Anxiety Disorder 7)**

**Purpose:** Screens for anxiety

**Format:** 7 questions, score 0-21

**Scoring:**

- 0-4: Minimal Anxiety
- 5-9: Mild Anxiety
- 10-14: Moderate Anxiety
- 15-21: Severe Anxiety

**Usage:** Used to assess anxiety symptoms over the past 2 weeks.

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**2. AUDIT (Alcohol Use Disorders Identification Test)**

**Purpose:** Screens for alcohol use disorder

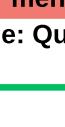
**Format:** 10 questions, score 0-40

**Scoring:**

- 8-15: Hazardous drinking, brief advice
- 16-19: Brief counseling, monitoring
- 20+: Diagnostic evaluation for alcohol dependence

**Usage:** Assesses the frequency and quantity of alcohol use.

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**3. AUDIT-C (Short Version)**

**Purpose:** Quick screen for alcohol use problems

**Format:** 3 questions, score 0-12

**Scoring:**

**≥4 for men, ≥3 for women: Requires further evaluation**

**Usage:** Quick screen to identify risky drinking habits.

Figure 23 TB Mental Health patient care pathway for Anxiety and Depression

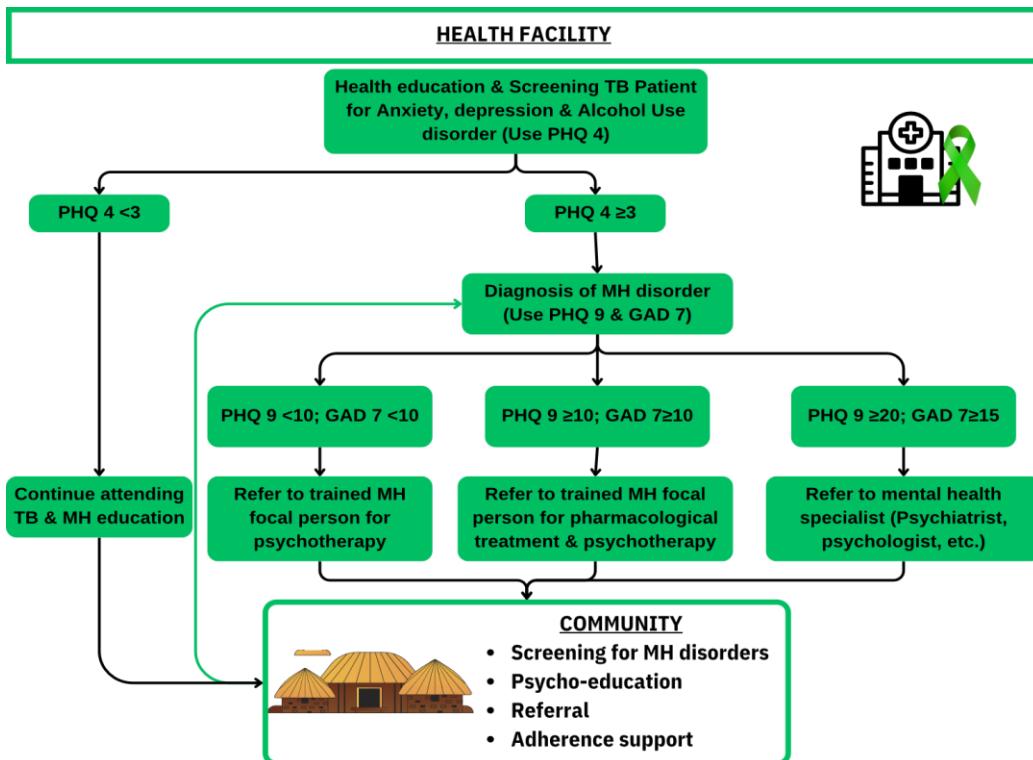
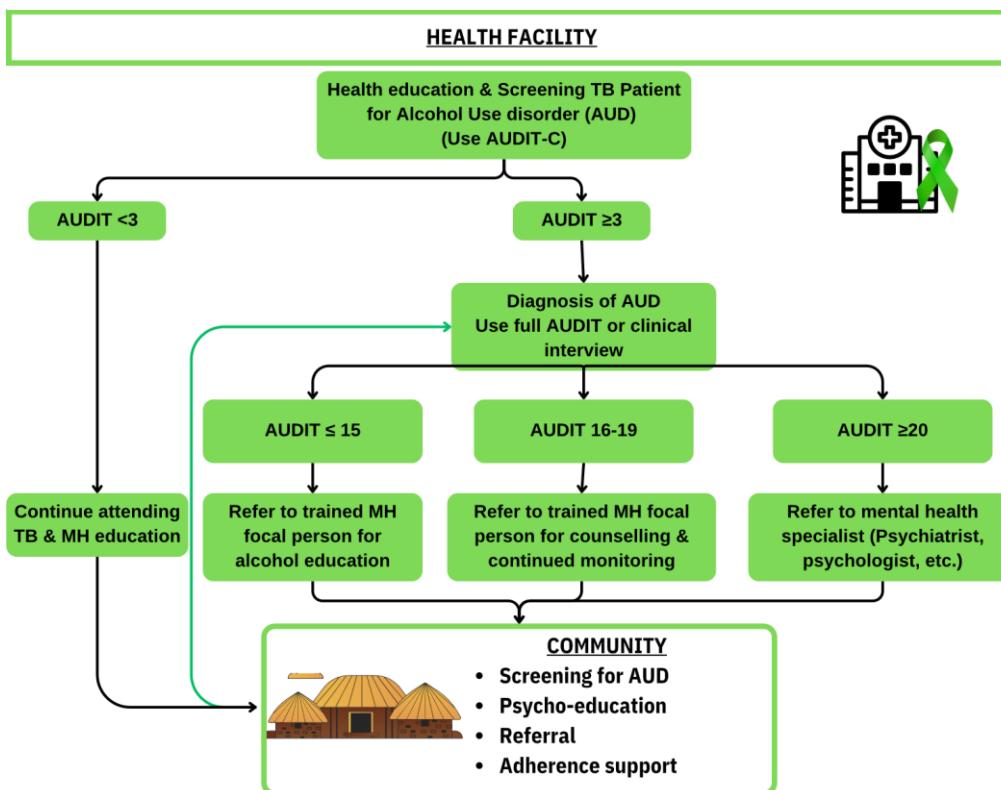


Figure 24 TB Mental Health patient care pathway for Alcohol Use Disorder



## TUBERCULOSIS AND DIABETES

Each year, 10 million new diabetes mellitus (DM) cases occur, with up to 5 million deaths from DM-related complications. DM increases the risk of TB by 2-3 times and worsens TB treatment outcomes, particularly when combined with HIV or smoking. DM is also a significant risk factor for multidrug-resistant TB (MDR-TB). TB can exacerbate DM by causing "stress-induced hyperglycaemia," complicating DM management.

In low- and middle-income countries, DM primarily affects middle-aged and older adults, though younger individuals are increasingly diagnosed. TB in DM patients may present atypically with faster progression, more chest and systemic symptoms, and higher-grade smear and culture positivity. Severity correlates with uncontrolled hyperglycaemia.

DM influences TB treatment in several ways:

**Sputum conversion:** DM can delay smear and culture conversion by 2-3 months.

**Adverse drug reactions:** DM is linked to higher risks of hepatitis and renal toxicity from TB medications.

**Treatment outcomes:** DM leads to worse TB treatment outcomes, possibly due to immunosuppression, drug-drug interactions, side effects, poor medication adherence, reduced drug bioavailability, or other factors. The risk of death during TB treatment is nearly doubled in DM patients, and adjusted models show a fivefold increased risk. DM also raises the likelihood of TB treatment failure and loss to follow-up.

### Does TB disease cause hyperglycaemia or DM?

TB does not cause DM although it may unmask those at risk of DM in the future. TB is associated with glucose intolerance and hyperglycaemia, both of which resolve automatically with TB treatment. TB also impairs glycaemic control among patients with previously known DM.

### Screening people with TB for DM

All adult TB patients should be screened for DM, with inquiries about typical symptoms (polyuria, polydipsia, polyphagia, weight loss, fatigue, slow wound healing). targeted testing should be done for those with risk factors prioritizing these subgroups in resource-limited settings:

- Those aged 40 years and above
- Those who are overweight or obese (with body mass index of 25 and above)
- Those with a family history of DM
- Those who are known to consume excessive amounts of alcohol
- Those with previous gestational DM or previous pre-DM

Logistically, it is easier to screen TB patients for DM at the time of diagnosis and registration as this increases the potential to identify and control DM at the start of TB treatment. The following are recommended:

1. TB patients should be screened for DM at the time of diagnosis and registration
2. TB patients with blood glucose levels consistent with pre-DM or DM should all be re-tested at the end of TB treatment and a decision made at that time on future management. This will avoid unnecessary, lifelong labelling of persons as having DM.

## **Diagnosing DM among TB patients**

Good history taking is a good starting point for diagnosis of DM. The challenge though is distinguishing the symptoms of DM (polyuria, polydipsia, polyphagia, unexplained weight loss, extreme tiredness, slow wound healing) from the symptoms of active TB disease. This is because some of the symptoms of DM may overlap or be explained by or be suppressed by TB.

Laboratory testing is critical in making a DM diagnosis. At the time of diagnosis and registration in the TB register, TB patients should be asked whether they are already known to have DM or whether they are on any DM treatment. For patients that do not have a diagnosis of DM should be offered a single RBG measurement at this time to identify those who are at risk and require further investigation with either FBG or HbA1c. The FBG and HbA1c tests are the two diagnostic tools most suited for use in the programmatic setting. Guidance on how to proceed depending on the results from RBS, FBG and HbA1c is as below:

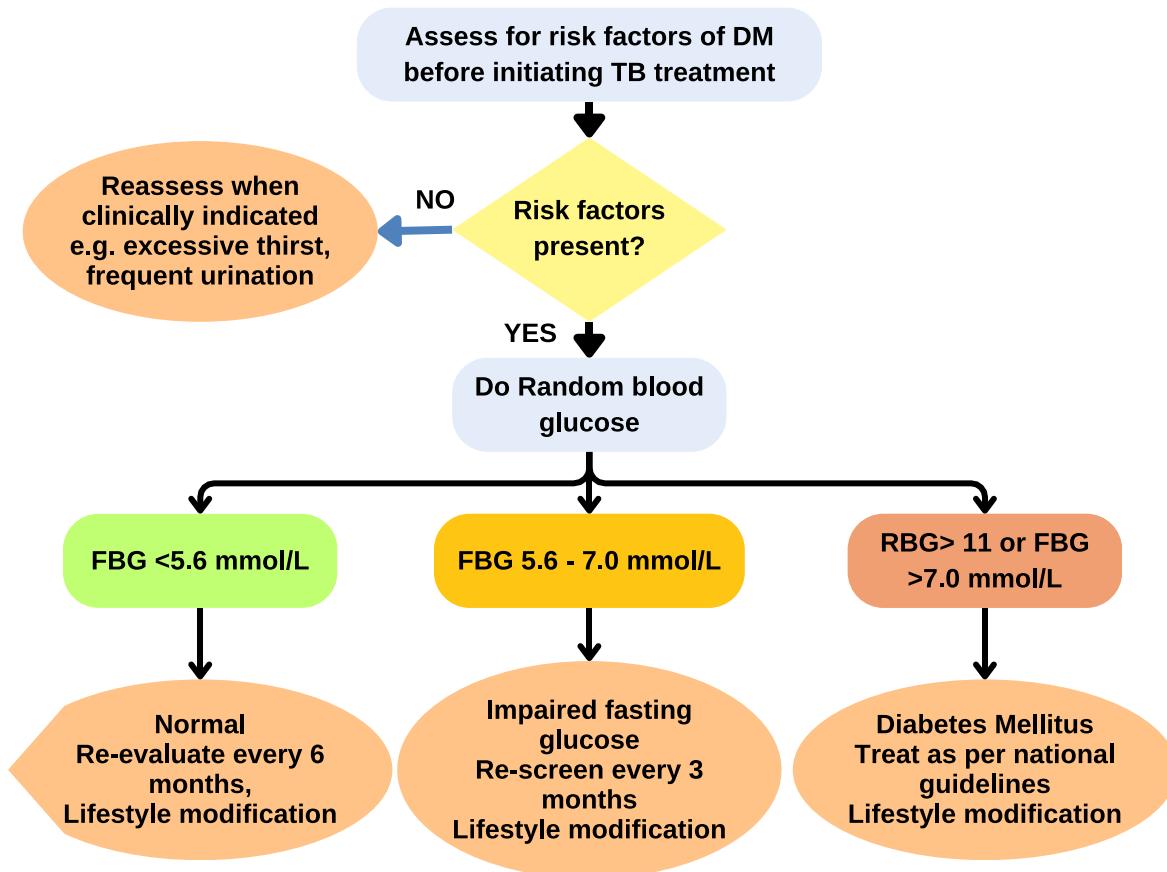
- i. If the RBG is  $<6.1\text{mmol/l}$  ( $<110\text{mg/dl}$ ): The TB patient is at low risk of DM and no further investigation is required
- ii. If the RBG is  $\geq6.1\text{ mmol/l}$  ( $\geq110\text{ mg/dl}$ ): The TB patient requires further investigation. This can be done on the same day using a glycosylated haemoglobin test (HbA1c) or the patient will have to come back on another day in a fasting state for a FBG test.
- iii. If the HbA1c  $\geq6.5\%$  ( $\geq48\text{ mmol/mol}$ ): The patient is diagnosed as having DM and recorded as such
- iv. If the FBG  $\geq7.0\text{ mmol/l}$  ( $\geq126\text{ mg/dl}$ ): The patient is diagnosed as having DM and recorded as such

Note:

- If the TB patient is diagnosed with DM, DM care should be provided from within the TB clinic for at least the first two weeks of TB treatment and if possible until the end of the initial intensive phase (2 months). This is to ensure that the TB patient is no longer infectious by the time he/she returns to the DM clinic. The medical team should be consulted at all times for guidance. If the patient has severe hyperglycaemic symptoms with an FBG  $>18\text{ mmol/l}$  ( $325\text{ mg/dl}$ ) or HbA1c  $>10\%$  then urgent DM specialist advice needs to be obtained.
- If the TB patient is found to have pre-DM, the patient should be informed about it and the result recorded. No further action is needed at this point in terms of DM care or support.
- If the TB patient is found to have a normal result, the patient is informed and the result is recorded and no further action is taken in terms of DM care or support
- All patients diagnosed with DM at the start of TB treatment need to have a repeat test done at the end of TB treatment to confirm whether or not they have DM

The algorithm for diagnosis of DM among TB patients is as below:

Figure 25 Algorithm for the diagnosis of DM among TB patients



### Screening people with DM for TB

Even though diabetes mellitus (DM) increases the risk of tuberculosis (TB), the numbers of patients with new active TB disease that can be identified in DM clinics is relatively small, thus TB screening in persons with DM should only be considered for systematic TB screening in countries with a TB prevalence of over 100 per 100,000 population. For guidance on the screening approach, please refer to Chapter 3.

The following is recommended:

- In settings with TB prevalence > 100 cases per 100,000 population, persons with DM should be screened for TB
- Persons diagnosed with new DM in high TB prevalence settings (>100 cases per 100,000 population) should be systematically screened as a one-off process at the time of diagnosis and registration in the DM clinic (an active case finding approach)
- Persons already in DM care in high TB prevalence countries (>100 cases per 100,000 population) should be educated about their increased risk of new and recurrent TB as well as the symptoms and signs of TB. Such patients should be advised to seek care if they think they might have active TB disease.

## **Management of diabetes mellitus during tuberculosis treatment**

The primary goal in managing diabetes during TB treatment is to improve TB outcomes while maintaining blood glucose control. TB treatment takes priority, but blood glucose levels must be carefully managed to prevent complications.

Metformin is the first-choice oral glucose-lowering drug for TB patients. Sulfonylureas can be used as add-ons or alternatives for those who cannot tolerate metformin, but their interaction with rifampicin limits their effectiveness.

The target for glycaemic control in TB-DM patients is an HbA1c of less than 8% or a fasting blood glucose (FBG) level below 10 mmol/L (180 mg/dL). Given the high cardiovascular risk in TB-DM patients, healthcare providers should incorporate cardiovascular risk assessment, lifestyle counselling, and appropriate prescriptions. Antihypertensives, statins, and antiplatelet therapy, including aspirin, should be considered early, particularly for patients with a history of cardiovascular disease.

Glucose monitoring is essential throughout treatment, with FBG being the preferred test. HbA1c can also be used but should not be repeated within the first 2–3 months of DM treatment. The frequency of monitoring depends on the severity of diabetes. In mild cases (HbA1c <10%), FBG should be checked every one to two weeks until stable. In severe cases (HbA1c ≥10%), more frequent monitoring is necessary. If fasting blood glucose cannot be measured due to non-fasting clinic visits, postprandial glucose testing should be used as an alternative.

*Table 51 Common glucose-lowering drugs used for managing DM in TB patients*

Characteristic	Metformin	Sulphonyl urea derivatives	Insulin
Drug of choice	First Choice	Add-on	Use if targets for HbA1c or FBG cannot be reached or if there is symptomatic hyperglycaemia
		Used in case there is a contraindication or intolerance to metformin	
Risk of hypoglycaemia	No	Yes	Yes
Starting dose (od=once a day; bid=twice a day)	500mg od or bid, titrated to a maximum of 2000 mg daily	Gliclazide 40-80mg Glibenclimide 2.5-5mg Glimepiride 1-2mg Glipizide 5mg OD	OD OD OD 10 units basal insulin per day as the starting point
Interaction with rifampicin	Not clinically relevant	Yes, 30-80% lower efficacy with rifampicin	None
Main side effects	Gastrointestinal Lactic acidosis	Hypoglycaemia	Hypoglycaemia
Use in reduced kidney function (GFR=glomerular filtration rate)	Dose adjustment if eGFR<45 ml/min Contraindication if eGFR <30 ml/min*	Increased risk of hypoglycaemia Preference gliclazide	Can be safely used
Cardiovascular events	Recognised benefit	Neutral	Neutral

\*eGFR=estimated glomerular filtration rate.

If measurement of eGFR cannot be done, metformin should not be given to patients with known chronic kidney disease without approval from their treating physician

The following steps should be carried out if a TB patient is diagnosed in a DM clinic:

1. The patient should be referred to the TB clinic to start TB treatment. TB medicines should be administered and monitored from the TB clinic until successful completion of therapy
2. Attendance at the DM clinic should be avoided during the intensive phase of TB treatment (the first two months). If DM control is difficult, contact the DM clinic for advice without referring the patient. If the patient does have to visit the DM clinic in the intensive phase, he/she should wear a surgical mask.

Care for TB patients with newly diagnosed or existing DM is outlined in Table 52 below.

*Table 52 Management of HbA1c or blood glucose at the start of TB treatment*

HbA1c or FBG at the start of TB treatment	TB patient diagnosed with new DM	TB patient already receiving treatment for DM
If HbA1c <8% or FBG <10.0mmol/l (189 mg/dl)	No further immediate action is taken; reassess blood glucose levels at 2 months and again at the end of TB treatment	No further action is taken; the patient continues on current medications for DM
If HbA1c ≥ 8% but less than 10% or FBG ≥ 10 mmol/l (180 mg/dl) but less than 15 mmol/l (270 mg/dl)	Start metformin 500 mg once a day, reassess in two weeks and increase the dose to 500 mg twice a day or refer if blood glucose levels have not improved	Intensify current glucose lowering treatment and reassess one-two weeks later
If HbA1c ≥ 10% or FBG ≥ 15 mmol/l (270 mg/dl)	Start metformin 500 mg twice a day and seek specialist advice	Seek specialist advice and consider the need for hospital admission for better glucose control

## Management of DM in Patients with HIV-associated TB

In patients with HIV-associated TB, there are a few issues which need special consideration (see Table 49 below). Drug-drug interactions are even more probable in these patients and toxicity profiles and side-effects of HIV, TB, and DM drugs might overlap.

*Table 53 Special considerations when co-managing HIV, DM and TB*

The issue	Special considerations	Action
TB-associated immune reconstitution inflammatory syndrome (IRIS)	Corticosteroids may be given for IRIS which can increase levels of hypoglycaemia	Monitor blood glucose and initiate glucose-lowering treatment if indicated
Drug-drug interactions	Many antiretroviral (ARV) drugs affect metabolism of glucose-lowering drugs, statins, anti-hypertensive drugs and anti-platelet drugs	Seek specialist advice about drug-drug interactions between ARV drugs
	Metabolism of most antiretroviral drugs is increased by rifampicin	
	Dolutegravir reduces metabolism of metformin	Preferably use raltegravir/ dolutegravir (in a double dose) or efavirenz (standard dose); avoid use of protease inhibitors Reduce metformin dose by 50%

The counselling at the end of TB treatment for DM patients is as follows:

- i. The need for continued DM care and monitoring
- ii. The increased risk and management of cardiovascular disease
- iii. The increased risk of TB relapse and what to do in case of renewed cough, fever, night sweats or weight loss

Note: Efforts should be made for effective referral to appropriate services for continued DM care.

### **Management of TB in people with DM**

The standard treatment regimens recommended for drug-susceptible and drug resistant tuberculosis (TB) remain unchanged with or without diabetes mellitus (DM).

When the person with DM is diagnosed with TB, either through bi-directional screening in the TB clinic or through bi-directional screening in the DM clinic, the treatment should always be administered, supervised and monitored in a TB clinic where the drugs are available and where health care workers are trained in the management of the disease and patient-centred care.

There are special considerations in managing DM patients with DS-TB. These are;

- i. Drug-drug interactions leading to reduced drug concentrations in the treatment of DM: Rifampicin increases hepatic metabolism of all oral sulphonyl urea drugs, thus reducing their plasma concentrations and making dose adjustments difficult. Insulin and metformin are largely unaffected by rifampicin and should be strongly considered if drug treatment of DM is needed. When oral sulphonyl urea drugs are used, weight-adjusted doses of TB drugs might be needed, although this is difficult to implement in routine programmatic practice
- ii. Drug-drug toxicity:
  - a. Isoniazid and DM: Peripheral neuropathy induced by both isoniazid and DM. It's advisable to use adjunctive pyridoxine at the start to counteract effects of isoniazid
  - b. Ethambutol and DM: Ethambutol-induced ocular effects and DM-induced retinopathy
  - c. Metformin and TB drugs: Gastrointestinal toxicity from metformin and TB drugs. Metformin may rarely cause lactic acidosis which needs to be considered and diagnosed if a TB patient deteriorates on therapy – the action is to stop metformin
- iii. Use of corticosteroids: Adjunctive corticosteroids for TB meningitis, TB pericarditis or IRIS in HIV-associated TB can lead to or aggravate hyperglycaemia. In this case, more frequent monitoring of blood glucose and appropriate adjustment is advised.

## TUBERCULOSIS AND ALCOHOL/SUBSTANCE ABUSE

Disorders due to substance use include both drug and alcohol use disorders and certain conditions including acute intoxication, overdose and withdrawal.

**Acute intoxication** is a transient condition following intake of a psychoactive substance resulting in disturbances of consciousness, cognition, perception, affect, or behaviour.

**Overdose** is the use of any drug in such an amount that acute adverse physical or mental effects are produced.

**Withdrawal** is the experience of a set of unpleasant symptoms following the abrupt cessation or reduction in dose of a psychoactive substance if it has been consumed in high enough doses and for a long enough duration for the person to be physically or mentally dependent on it. Withdrawal symptoms are, essentially, opposite to those that are produced by the psychoactive substance itself.

**Harmful use** is a pattern of psychoactive substance use that damages health. This damage may be physical, e.g., liver disease, or mental, e.g. episodes of depressive disorder. It is often associated with social consequences, e.g., family or work problems.

**Dependence** is a cluster of physiological, behavioural, and cognitive phenomena in which the use of a psychoactive substance takes on a much higher priority for a given individual than other behaviours that once had greater value. It is characterized by a strong craving to use the substance and a loss of control over its use.

Globally, people who use drugs remain stigmatised and criminalised. This leads to health disparities as well as increased rates of TB, often combined with HIV and viral hepatitis.

People that misuse drugs or alcohol have an increased risk of TB. This is because:

- Alcohol and drugs damage a person's body and weaken their defences against illnesses such as TB
- They may be around other people who have infectious TB but don't know it
- They may not eat a diet that provides all the nutrients they need to stay healthy
- They may spend time in places where it's easier for TB to spread, such as crowded or poorly ventilated homes or social venues

The TB symptoms could be masked by the alcohol and drugs. Further, someone with a substance misuse problem may also find it difficult or be reluctant to access healthcare, or adhere to their medication. This increases the risk of transmission in the community as well as increasing risk of developing drug-resistant TB.

TB treatment in the alcohol and substance abusers is complicated due to:

- TB medication can lead to side effects such as liver toxicity, which is particularly dangerous for people who drink too much alcohol
- Injecting drug users are at risk of co-infection with viral hepatitis and/or HIV, which require careful monitoring and alternative drug-regimen.

Currently a range of treatment options with proven effectiveness is available for management of alcohol and drug use disorders. These range from screening and brief interventions for risky patterns of alcohol consumption/drug abuse to pharmacological and structured psychosocial interventions.

There are two major public health approaches that are justified:

1. The first approach is related to systematic screening for alcohol use and early identification of alcohol use disorders in all patients engaged with prevention and treatment services for TB. Health professionals in these settings should be trained to identify not only alcohol use disorders, but also patterns of alcohol use associated with increased risk of negative health consequences including TB-related risks.
2. The second approach is related to active screening and identification of TB cases among people with alcohol use disorders, including those enrolled in special treatment programmes for alcohol dependence.

Management of TB and alcohol use disorder comorbidity requires intensive patient support and social protection measures.

### **Common presentations of disorders due to substance abuse**

- i. Appearing affected by alcohol or other substance (e.g., smell of alcohol, slurred speech, sedated, erratic behaviour)
- ii. Signs of recent drug use (recent injection marks, skin infection)
- iii. Signs and symptoms of acute behavioural effects, withdrawal features or effects of prolonged use
- iv. Deterioration of social functioning (i.e., difficulties at work or home, unkempt appearance)
- v. Signs of chronic liver disease (abnormal liver enzymes), jaundiced (yellow) skin and eyes, palpable and tender liver edge (in early liver disease), ascites (distended abdomen is filled with fluid), spider naevi (spider-like blood vessels visible on the surface of the skin), and altered mental status (hepatic encephalopathy)
- vi. Problems with balance, walking, coordinated movements, and nystagmus
- vii. Incidental findings: macrocytic anaemia, low platelet count, elevated mean corpuscular volume (MCV)
- viii. Emergency presentation due to substance withdrawal overdose, or intoxication. Person may appear sedated, overstimulated, agitated, anxious or confused

### **Management of Tuberculosis in patients with Alcohol/Substance abuse**

#### **i. Screening**

Individuals with alcohol/drug abuse disorders are at an increased risk of TB disease and should thus be systematically screened for TB. The usual screening approaches used for other individuals can still be used for individuals with alcohol and drug abuse issues.

#### **ii. Treatment**

Once a diagnosis of TB has been made, the individual should be supported to complete treatment. The treatment options available for TB are the same as for all other individuals. Alcohol just like some TB drugs could lead to liver toxicity and its important liver function is monitored through careful history taking and examination, and if resources allow, through liver function testing.

## **Management of Alcohol/Substance Abuse in Patients with Tuberculosis**

Managing alcohol and substance abuse in TB patients involves both non-pharmacological and pharmacological interventions:

### **1. Psychosocial Interventions**

#### **a) Psychoeducation:**

- Disorders due to substance use can often be treated effectively.
- Discuss substance use in a non-judgmental way to reduce feelings of embarrassment or shame.
- Encourage patients to return for further discussion if needed.
- Emphasize that success in reducing or stopping substance use is more likely if it's the patient's own decision.

#### **b) Motivational Interviewing (Brief Intervention):**

- Motivational interviewing fosters a non-judgmental environment, encouraging patients to reflect on their substance use.

Key techniques include:

- i. **Feedback:** Provide personalized feedback on the risks and harms associated with the patient's substance use.
- ii. **Taking Responsibility:** Encourage the patient to take responsibility for their choices.
- iii. **Reasons for Use:** Explore why the patient uses substances, including any links to mental health issues or stress.
- iv. **Consequences:** Discuss the perceived consequences of their substance use, both positive and negative.
- v. **Personal Goals:** Explore whether substance use is preventing the patient from achieving their personal goals.
- vi. **Discussion:** Discuss the contradictions between the patient's goals and the consequences of substance use.
- vii. **Options:** Present realistic options for change and collaborate on a course of action.
- viii. **Support:** Offer support and provide information on further steps such as detoxification, psycho-social support, or additional reviews.

#### **c) Strategies for Reducing and Stopping Use:**

- **Identify Triggers:** Discuss situations or emotional cues that prompt substance use and how to avoid them.
- **Safe Practices:** Encourage the patient to avoid keeping substances at home and suggest healthier coping mechanisms for emotional triggers.

#### **d) Harm Reduction and Treatment for Related Conditions:**

Encourage safe practices such as avoiding driving when intoxicated.

##### **i. For opioid users:**

- a. Provide naloxone to family members in case of overdose.

##### **ii. For those who inject drugs:**

- Educate about the risks of intravenous drug use (e.g., infections, HIV/AIDS, Hepatitis B and C) and promote safer injection practices.
- Ensure access to sterile needles and syringe exchange programs if available.
- Offer regular testing for blood-borne diseases and provide Hepatitis B vaccination.
- Promote condom use and treatment options for HIV/AIDS and Hepatitis patients.
- By integrating these strategies, healthcare providers can support TB patients in overcoming substance abuse while managing their tuberculosis treatment effectively.

## **Treatment of co-morbidities**

- Have a low threshold for screening for TB in people who have disorders due to substance use
- Consider investigations for and treatment of sexually transmitted diseases.

## **Management of alcohol withdrawal**

It is important patients suffering from alcohol withdrawal symptoms are well managed. The following should be done.

- Provide as quiet and non-stimulating an environment as possible; well-lit during the day and lit enough at night to prevent falls if the person wakes up at night
- Ensure adequate fluid intake and that electrolyte requirements are met, such as potassium and magnesium
- Address dehydration: Maintain adequate hydration including intravenous hydration, if needed, and encourage oral fluid intake. Be sure to give thiamine before glucose to avoid precipitating Wernicke's encephalopathy. To prevent Wernicke's encephalopathy, all persons with a history of chronic alcohol use should be given thiamine 100 mg p.o. per day
- Pharmacological Intervention (+/-): When appropriate, treat alcohol withdrawal symptoms. In the case of planned detoxification, prevent withdrawal symptoms using diazepam. The dose and duration of diazepam treatment varies according to the severity of the withdrawal
  - i. Administer diazepam at an initial dose of up to 40 mg daily (10 mg four times a day or 20 mg twice a day) for 3-7 days, p.o. Gradually decrease the dose and/or frequency as soon as symptoms improve. Monitor the person frequently, as each person may respond differently to this medication
  - ii. In the hospital setting, diazepam can be given more frequently, (i.e. hourly), and at higher daily doses, up to 120 mg daily for the first 3 days p.o., if necessary, and based on frequent assessment of the person's withdrawal symptoms and mental status
  - iii. In persons with impaired hepatic metabolism, (i.e. persons with signs of liver disease or the elderly), use a single low dose initially of 5-10 mg p.o., as benzodiazepines may have a longer duration of action in these populations. Alternatively, a shorter acting benzodiazepine such as oxazepam may be used instead of diazepam

CAUTION: Use caution when initiating or increasing the dose of benzodiazepines, as they can cause respiratory depression. Use with caution in persons with respiratory disease and/or hepatic encephalopathy.

## **CHAPTER 9: TUBERCULOSIS INFECTION CONTROL**

### **Tuberculosis Infection Control (TB IC) measures**

Effective IPC measures are a critical part of the quality of health service delivery to achieve people-centred, integrated universal health coverage. TB IC is a combination of measures and work practices aimed at minimizing the risk of TB transmission within populations or congregate setting. TB infection control measures should complement general infection control efforts.

The set of TB infection control measures that should be implemented at health facility level is outlined below:

#### **Administrative controls**

These controls are the first and most important component of any IPC strategy. The measures consist of specific interventions aimed at reducing exposure and therefore reducing transmission of *M. tuberculosis*. They include activities like triage and patient separation systems (e.g., management of patient flows to promptly identify and separate presumptive TB cases), prompt initiation of effective treatment and respiratory hygiene.

##### **i. Triage**

Triage of people with signs and symptoms of TB is recommended to reduce transmission to health workers and other persons attending the health care facilities. Implementation of any triage system needs to be focused on fast-tracking of presumed TB cases and on minimizing time in the facility.

Triage could also be implemented in other settings with a high risk of *M. tuberculosis* transmission where persons with presumed TB may congregate. Such settings include long-term care and correctional facilities e.g., prisons, regardless of the burden of TB disease.

The administrative controls could also be implemented at the level of the community. Community health workers can promptly identify presumptive TB cases at the community level and refer them for TB diagnosis. This ensures early detection of TB and ultimately reduces the risk of transmission in the community in general.

##### **ii. Patient separation systems**

Respiratory separation/isolation of people with presumed or demonstrated TB is recommended to reduce transmission of TB to health workers or other persons attending health care facilities.

The health care system must implement available patient care and support measures before resorting to isolation of any person. In situations where isolation is required, this should be decided in consultation with the patient, and carried out in medically appropriate settings.

Patients who are admitted to isolation express higher rates of anxiety and depression than other hospitalized subjects and it is thus important that these patients are informed of the rationale for respiratory separation or isolation measures, and that psychological support is provided to them.

In scenarios where patients are considered to be infectious and care is being provided at decentralized facilities (e.g. patient's home), patients and their family members providing care should receive clear guidance and indications on IPC.

### **iii. Prompt initiation of TB treatment**

Prompt initiation of effective treatment of people with TB disease is recommended to reduce M. tuberculosis transmission to health care workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

### **iv. Respiratory hygiene (including cough etiquette)**

Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce Tuberculosis transmission to health care workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

## **Administrative TB-IC in General Health Facilities**

The staff in the general clinics should take the following steps to ensure infection control:

- i. Develop a "triage" system whereby known TB patients or persons likely to be presumptive TB patients and their accompanying contacts are promptly identified, isolated in a well- ventilated place upon arrival at a health facility clinic and are fast tracked to diagnosis and treatment follow up. Fast tracking of these patients, reduces the time they spend in a health facility thereby minimizing TB transmission. The health workers do this by asking the patients questions such as: Who among you has a cough that has lasted for two or more weeks? Is there anyone among you who has ever been treated for TB? To minimize stigma, explain to patients that safety without stigma is the goal of IC and that screening for, and prevention of TB transmission is part of providing quality health care.
- ii. Educate patients about cough hygiene: When you cough, cover your mouth and nose with a handkerchief or paper tissue. If you do not have a handkerchief or paper tissue, turn to the inside of your arm, and cover your nose and mouth with it (See Figure 12). This figure should hang on the wall in the clinic. If a face mask is available, give to known or presumptive TB patients to wear over their mouth and nose.
- iii. Even if the mouth is covered, tell the patients always to turn away from facing other people when coughing, whether the mouth is covered by a handkerchief, tissue, face mask or an arm.
- iv. Identify an area of the ward or isolation room that is separated from the main ward and designate it for diagnosed and presumptive TB patients. This area should be a well-ventilated area of the ward.
- v. Develop written instructions on keeping windows and doors open for ample circulation of air. This instruction should clearly indicate time to open windows and doors, and the patients should be informed about this when first admitted and constantly reminded about it.
- vi. Transport known and presumptive TB patients with window open or patients seated in a separate cabin
- vii. Designate TB IC responsibilities clearly and correctly and at same time communicate with all relevant partners and stakeholders.

## **Administrative TB-IC Measures in Tuberculosis clinics and wards**

- i. The staff in the TB clinics should:
- ii. Regularly educate TB patients about the importance of preventing transmission of TB in the wards and at all outpatient clinics.
- iii. Ask the patients to identify anyone with two or more weeks of cough in their family or community so that they can be examined for TB disease.
- iv. Educate the patients about cough hygiene. Instruct patients to cover their mouths and noses with a handkerchief (Figure 21). This is to prevent further transmission between patients, attendants and staff. Explain to them that this is for the benefit of everybody and should not make them feel bad or discriminated against.
- v. Sputum produced after coughing should be placed in a screw capped container, disinfected after use and place in a highly infectious waste bin before final disposal.
- vi. Identify known or suspected drug-resistant TB patients and separate them from other TB patients.
- vii. Develop and hang health education messages on the ward and clinic walls.
- viii. Develop written instructions on keeping windows and doors open for free circulation. This instruction should clearly indicate time to open windows and doors, and inpatients should be informed about this when they are first admitted and constantly reminded about it.
- ix. All staff should periodically be screened for symptoms of active TB disease. Schedule TB testing for all staff at least once a year using Xpert MTB/Rif for those symptomatic and or CXR.
- x. Offer staff voluntary, confidential HIV counselling/testing, and annual repeat testing if HIV negative on previous occasions.
- xi. Document both TB and HIV results in staff member's occupational file. HIV positive staff should be offered Anti-retroviral therapy and Isoniazid preventive therapy (IPT) and should not be deployed high-prevalent TB settings. Offer HIV preventive services to HIV negative health care workers.

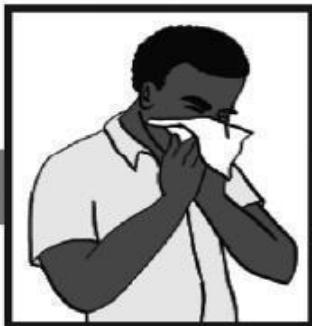
*Figure 26 : Illustration showing cough hygiene - Adapted from WHO*

### **Cover your cough or sneeze.**



**Cough or sneeze into  
your arm.**

**or**



**Use a tissue and then  
throw away...**

## Managerial controls

### Managerial activities at health facility level

- To have effective and smooth implementation of TB IC measures at a health facility, there is need have managerial activities in place. These activities are normally spear headed by a TB Infection control committee. The activities the committee is involved in constitute the basis for setting up and implementing other controls at the facility level. These roles of the committee include:
- Conduct of TB IC facility assessment to inform TB IC plans. The assessment should consider type of clinical services offered by the facility (e.g., TB, HIV, general services, etc.), the number of beds, the number of employees, location of facility and the different clinics, disease prevalence in the community, volume of patients and the risks of exposure to employees and patients prior to the creation of the action plan.
- Development of a facility specific TB IC plan (based on the above assessment) that is time bound with a budget (that includes human and material resources), policies and procedures that ensure sustained and effective implementation of the TB IC measures outlined below. The plan should cover radiology, sputum induction and cough inducing procedures, surgical autopsy suites, Intensive case areas and other high-risk areas/ procedures.
- Organization of TB IC at a facility level
- Consideration of usage of available space, needed renovation/remodelling or construction to optimize implementation of TB IC
- Conduction of onsite surveillance of TB among Health Care Workers (HCWs). HCWs are all people engaged in actions whose primary intent is to enhance health and these include only paid workers and cleaners working in a health facility.
- Conduction of advocacy, communication and social mobilization for HCWs, patients and visitors.
- Conduct of monitoring and evaluation of the set of TB IC measures at this facility
- Participation in TB IC operational research

## Environmental controls

### Environmental controls at facility level

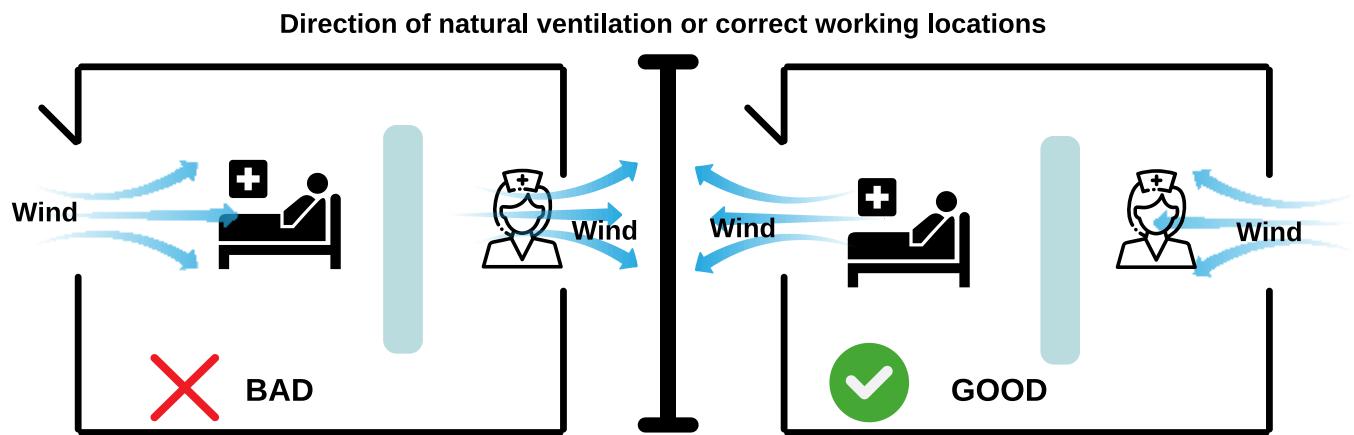
Environmental controls reduce the concentration of infectious droplet nuclei in the air. Air can be made less infectious through the use of three principles: dilution, filtration and disinfection. Sufficient air exchange of about  $\geq 8-12$  air changes per hour (ACH) reduces the concentration of droplet nuclei in the room air.

Environmental control measures can be achieved by using special ventilation systems to maximize airflow rates or filtration, or by using germicidal ultraviolet (GUV) systems to disinfect the air. Ventilation systems can also be used to control the direction of airflow to reduce the spread of infection; e.g. opening of windows and mechanical ventilation through use of fans – ceiling, floor and wall exhaust fans which force air exchanges and to drive air flow by generating negative pressure in the room thereby driving bad air out and fresh air in), mixed-mode ventilation (uses both mechanical and natural ventilation), HEPA filtration, air flow by negative pressure mechanism and Ultraviolet Germicidal Irradiation (UVGI).

These all have both advantages and disadvantages, therefore, the choice of any of the above environmental measures is based on available technology, building design, local climatic factors, specialty of the health facility and technical capacity to install these devices as well as resources to procure and maintain them. In our settings and in most health care facilities, use of natural ventilation that achieves  $\geq 8-12$  air changes per hour (ACH) is adequate and cost effective.

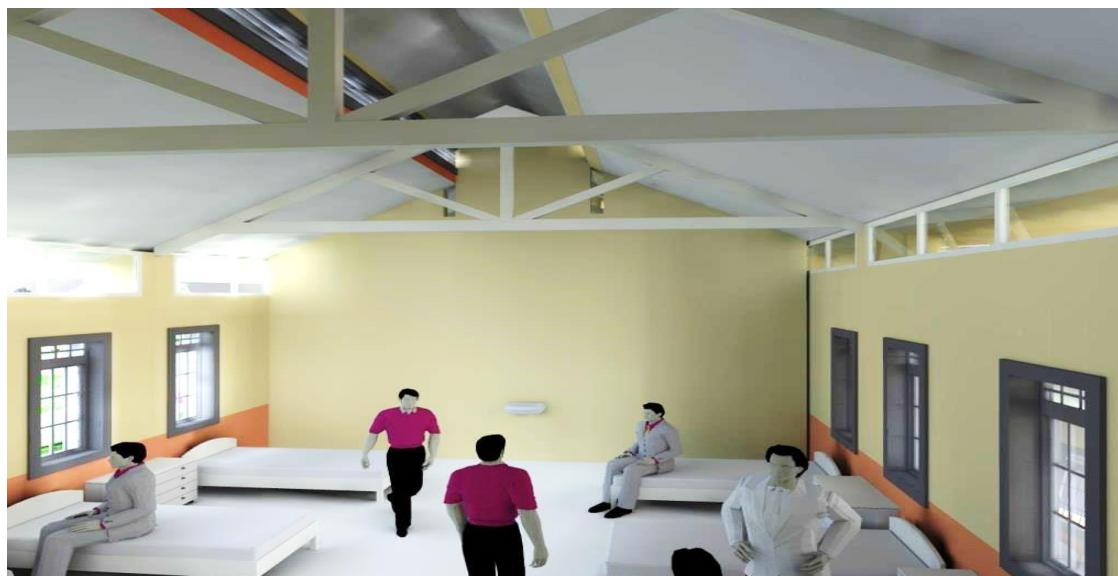
Natural air movement should be monitored to determine the sitting arrangement in consultation rooms between patients and HCWs as illustrated in Figure 27 below.

*Figure 27 Clinic sitting arrangement*



In addition to paying attention to sitting arrangement to reduce the risk of exposure, the inter-bed distances in TB risk areas like TB wards and medical wards etc. have to be kept at 2.5 meters (measured from the centre of one bed to the centre of the next bed to prevent overcrowding, thereby allowing improved air circulation within facility wards. The bed arrangement should be with head-to- foot, instead of head-to-head (Figure 18). Furniture should be positioned in a way that does not interfere with the free flow of fresh air within a clinic or facility ward.

*Figure 28 Bed arrangement in a TB ward*



## **Personal TB-IC Measures for health workers**

In order to control TB infection among health care workers, they should:

- i. Learn the symptoms of presumptive TB. Should any health worker have a cough that lasts for 2 or more weeks that is associated with fevers, loss of weight and reduced appetite, such a health worker should report for examination to diagnose TB.
- ii. Be encouraged to know their HIV status and, if positive, must not be assigned to work in TB wards or clinics.
- iii. Whenever possible, health workers should be examined to exclude TB twice a year.
- iv. Use personal protection exposures (PPE) such as N95 mask whenever possible during work within TB wards or clinics. Wearing of N95 respirators is a must while working in drug resistant TB (DR-TB) facilities or attending to patients with or suspected to have DR-TB. Those working in areas such as x-ray rooms and the mortuary should be prioritized for N95 masks. For N95 masks to be effective a fitting test is required.

## **Disinfection and disposal of sputum**

- Health workers must ensure that after instructing the patients how to obtain a sputum specimen, the patient goes to perform the act of producing the specimen in an open place away from the laboratory and other people. When a designated area for taking sputum specimen is available, the patient is sent to that area.
- Sputum of inpatients that is collected for disposal should be in a sputum mug or a plastic screw cap container. This container should have disinfectant liquid (5% Lysol) poured into it before the sputum material is put in it. Sputum from all the inpatients wards should be collected into one big container, further disinfected, and then disposed of according to standard guidelines for disposal of biological waste.

## **TB-IC in congregated populations**

A congregated population is a group of people staying close in proximity to each other – for example, school children, refugees, soldiers and prisoners. The measures described below are useful for controlling TB infection in such a population:

- i. Plan for and develop TB and HIV/AIDS collaborative activities for the institution with a congregated population.
- ii. Establish TB diagnostic and treatment services.
- iii. Educate population and staff on relationship between TB and HIV infection, so that they can recognize TB suspects.
- iv. Advocate for an isolation unit for patients diagnosed with TB or suspected to have TB.
- v. Consider “active screening” of the immediate group members for TB, when new pulmonary TB sputum smear-positive is diagnosed.

## **TB-IC in Households**

TB-IC activities and measures used in health care facilities also apply to households (HHs). All stakeholders must be involved. Policy makers, community leaders, patients and their families have to appreciate the importance of TB-IC in HHs. TB-IC in households begins with ensuring early diagnosis of TB. Patients and their family members are the first to notice TB symptoms. They should immediately ensure that care is sought. Once a diagnosis is made, adherence to treatment is key to TB- IC. Furthermore, practices to reduce the spread of TB should be implemented. These practices include:

- Houses should be adequately ventilated, particularly rooms where people with infectious TB spend considerable time (natural ventilation may be sufficient to provide adequate ventilation).
- Anyone who coughs should be educated on cough etiquette and should follow such practices always.
- While smear positive, TB patients should spend as much time as possible outdoors, sleep alone in a separate, adequately ventilated room and spend as little time as possible in public places or in public transport.
- While smear or culture positive, MDR-TB patients who cough should always practice cough etiquette (including use of face masks) when in contact with people.
- Ideally, health service providers should wear respirators when attending patients in enclosed spaces.
- Ideally, family members living with HIV, or family members with strong clinical evidence of HIV infection, should not provide care for infectious MDR-TB patients. If there is no alternative, HIV positive family members should wear respirators.
- Children below five years of age should spend as little time as possible in the same living spaces as culture-positive MDR-TB patients. Such children should be followed up regularly with TB screening for two years and, if positive, drug-susceptibility testing must be done.
- When conditions do not exist to minimize risk of TB infection in a household, XDR-TB patients should be admitted to a specialized healthcare facility.
- Household members of any TB patients should be encouraged to get screened for HIV and TB and be given appropriate (preventive) therapy.
- If possible, HIV-positive family members, or family members with a strong clinical evidence of HIV infection, should not share a household with culture positive XDR-TB patients.
- If possible, renovation of the patient's home should be considered, to improve ventilation (e.g. building of a separate bedroom, or installation of a window or wind catcher – "Whirly bird"– or both).

## **Hierarchy of Infection control measures**

Infection control measures can also be looked at as being in a form of hierarchy. This hierarchy highlights the relative importance of infection control measures. The hierarchy is:

1. **1st priority - Administrative controls (workplace):** This is the most important level, which aims to stop/prevent the release of droplet nuclei into the air thereby reducing the exposure of the HCWs, patients and visitors to M. tuberculosis.
2. **2nd priority - Environmental (Engineering) controls:** These actions complement the administrative measures. They reduce the concentration of droplet nuclei in the air in high-risk areas.
3. **3rd priority - Personal protective measures:** These measures protect individual persons especially HCWs from releasing or inhaling the droplet nuclei.

## **CHAPTER 10: SURVEILLANCE, MONITORING, EVALUATION AND RESEARCH (SMEAR)**

**Definitions:**

### **Surveillance**

Surveillance is the ongoing systematic collection, analysis, interpretation, and dissemination of data about a health-related event. It is a critical component of successful TB control, providing essential information needed to do the following:

1. Determine TB & leprosy patterns and trends of the disease.
2. Identify sentinel events, such as potential outbreaks, recent transmission, multidrug resistance, and deaths.
3. Identify high-risk populations and settings/ hotspots
4. Establish priorities for control and prevention activities.
5. Strategically plan use of limited resources

At NTLP, the electronic case-based surveillance system (eCBSS) has been deployed. Under this we estimate the TB incidence, TB prevalence, drug resistance survey and cross border surveillance.

Routine weekly TB surveillance is done to monitor the trends and the TB epidemic in the country. Emergency responses based on the TB prevalence data are also conducted. Tracking of the TB treatment outcomes is also done under surveillance.

### **Monitoring**

Monitoring is continuous process of data collection to track how a program/activity is being implemented in relation to an activity plan. Routine tracking of the key elements of program/project performance, usually inputs and outputs is achieved through record keeping, regular reporting and surveillance systems. Therefore, monitoring is useful to:

- Track progress toward the set performance standards (targets)
- Determine whether activities are proceeding according to plan or need adjustment during the intervention or implementation in order to realize desired outputs or outcomes

### **Evaluation**

Evaluation is the systematic assessment of an on-going or completed service, project, program or policy, involving its design, implementation and results to determine its worth or merit; determine how well the project or program has met set objectives and/or the extent to which changes in outcomes can be attributed to the interventions, project or program.

Impact evaluation is the process of measuring of how much things have changed because of the intervention(s) implemented. Because there are many factors that cause things to change, a formal evaluation tries to demonstrate how much a specific intervention contributed to the change.

## **Research**

Research is defined as the creation of new knowledge and/or the use of existing knowledge in a new and creative way so as to generate new concepts, methodologies and understandings. This could include synthesis and analysis of previous research to the extent that it leads to new and creative outcomes. The Smear has a focal person for research that coordinated and ensures NTLP encompasses pure and strategic basic research, applied research (usually to investigation undertaken to acquire new knowledge but directed towards a specific, practical aim or objective) and experimental development.

### **Importance of surveillance, monitoring, evaluation and research**

The role of SMEAR in the MoH M&E unit will be enhanced to address the expanding information needs of the NTLP and partners. The unit will work very closely with the Directorate of Health Governance and Regulation and Division of Health Information. This will ensure that the Tuberculosis & Leprosy data systems are functional and accessible and will improve data demand and timely data use for decision-making. All data from facility and non-facility-based interventions will be deposited in the data warehouse at the Ministry of Health. The unit will also spearhead the centralized access and utilization of programme information through the Ministry of Health Observatory. Additionally, it will continue to act as the secretariat to the TB SMEAR technical working group of the NTLD and partners to ensure conformity to the “one M&E framework.”

The key M&E unit tasks include:

- i. Producing periodic reports linked to the NTLD strategic and annual plans.
- ii. Conducting data analytics and trends analyses
- iii. Ensuring that data collection systems and tools are in place and functional.
- iv. Strengthen M&E capacity at subnational level.
- v. Planning and budgeting for surveillance, monitoring and evaluation and research.
- vi. Ensuring periodic performance reviews are done.
- vii. Ensuring coordination and oversight for M&E activities among partners.
- viii. Engage stakeholders to utilise data to inform programs, planning and policy.
- ix. Conducting data quality assurance and assessments, service delivery, client satisfaction and other evaluations.
- x. Ensuring functionality and maintenance of electronic platforms for data capture and reporting e.g., eCBSS, TBINFO.
- xi. Maintaining a meeting recommendation implementation tracking plan, which tracks review and evaluation recommendations, agreed follow-up actions, and status of these actions.
- xii. Timely detections and investigation of TB and Leprosy outbreaks through early warning mechanisms.

Table 54 Monitoring and evaluation activities by operational level

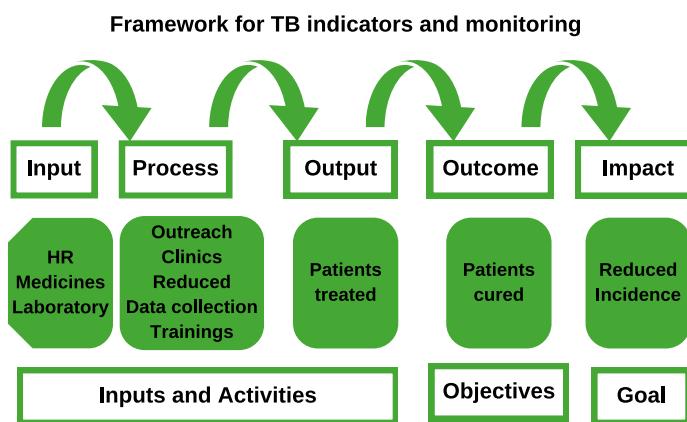
Level	Monitoring activities	Evaluation activities
Facility	Keeping accurate and complete records monitoring tools	Measurement of facility performance against set targets on TB case finding, case holding, DOT and TB-HIV collaborative activities (e.g., TPT, ART, CPT, TBIC coverage)
	Reviewing and updating the collected records regularly	
	Compiling and analysing data on TB indicators such as: TB case finding, case holding, DOT, TB-HIV collaborative activities, TB contact tracing activities, TPT and other activities of the TB program	
District	Carrying out support supervision	Measurement of district performance against district set targets on TB case finding, case holding, DOT, and TB-HIV collaborative activities (TPT, ART, CPT, TBIC coverage)
	Reviewing and updating the collected records regularly	
National	Compiling data on key TB indicators: TB case finding, case holding, DOT, TB-HIV collaborative activities and other activities of the TB programme	Conduction of TB surveys to determine prevalence, and incidence, community awareness
	Carrying out support supervision	Measurement of national performance against set targets on TB case finding and case holding, DOT, TB-HIV collaborative activities (TPT, ART, CPT, TBIC coverage)

### How TB SMEAR works

TB SMEAR is a structured system for data collection, reporting, analysis, and supervision, designed to track progress in TB control and support decision-making. Key features include:

- Data Collection and Reporting: Systematic and consistent gathering of data on TB cases and outcomes.
- Promotion of Data Use: Encourages the demand for data and its use for decision-making and program improvements.
- Evidence-Based Decision Making: Generates data that informs TB policy decisions, design, and implementation of control activities by the National TB Program (NTLP).
- Tracking Program Progress: Works within a defined framework to track progress and demonstrate the results of TB control efforts.
- Indicators for Monitoring: Uses indicators to measure key aspects of TB service delivery, such as TB case detection and treatment outcomes, aligned with the NTLP's national strategic plan.
- M&E Plan: The NTLP's M&E plan is based on a monitoring framework that tracks the progress of TB control and the implementation of the National Strategic Plan.
- Comprehensive Indicator System: The M&E system includes indicators derived from inputs, processes, outputs, outcomes, and impact, forming the basis for assessing NTLP performance.

Figure 29 Framework for TB indicator and monitoring



## Data reporting system

The data reporting system is organized from community level, to health centres, district and subsequently national level through the district health information system (DHIS2). Standard operating procedures (SOPs) are in place to guide health facility, district, regional and national level officers in data completeness, quality and utilization for performance improvement at different levels.

TB service data reporting utilizes two (2) systems:

- By facilities through DHIS2 to the Ministry of Health
- By the district, TB and leprosy supervisors (DTLS) through the Regional TB and Leprosy focal persons, to the NTLP using the TB quarterly report form

## Quarterly reporting procedure

The table below guides on the timelines for reporting at each level and the key deliverables at each level. It has key dates that personnel are supposed to adhere to ensure timely submission, review and meaningful use of data.

*Table 55 Quarterly reporting procedure*

Days after end of quarter	Activity	Level	Key deliverable(s)	Responsibility
30 <sup>th</sup> June, September, December, March	Pre-reporting meeting	National, regional, district	District and regional teams oriented on procedure of reporting and timelines	TB SMEAR
1 <sup>st</sup> to 15 <sup>th</sup> (July, Oct, Jan, Apr)	Report compilation, district data harmonization and validation meeting (DDVM) and entry into DHIS2	Health facility, District	All HMIS 106A reports compiled, validated with DTLS and entered into DHIS2	Health facility staff, DTLS, Biostatisticians
16 <sup>th</sup> and 21st (July, Oct, Jan, Apr)	Review for data quality Prepare national level analytics	National	Data Quality issues shared National, regional and district analytics shared National, regional and district analytics shared	TB SMEAR
22nd July, Oct, Jan, Apr)	Conduct national performance review meeting	National	Indicator Performance for national resolutions to be cascaded to the regional levels	TB SMEAR
25 <sup>th</sup> to 31 <sup>st</sup> (Last week of July, Oct, Jan, Apr)	Conduct Regional Performance Review Quarterly Meetings (RQPRM)	Regional	Understanding issues raised by TB SMEAR; discuss issues arising from the region; arrive at resolutions & Action plans to improve performance	NTLP Central Team leaders
3 <sup>rd</sup> or 4 <sup>th</sup> week of the second month (Aug, Nov, Feb, May)	Quarterly Data and Knowledge Management meetings	National	Submit regional explanations of national issues and issues discussed in QRM; regional Resolutions & Action plans shared at NTLP level to inform management decisions; Final report on national and regional issues; resolutions from regional performance review meetings and national level recommendations and action plan for dissemination in a report, Partnership meeting, NCC and beyond	TB SMEAR; This will feed into the facility sampling and checklists for Support Supervision

## **District level data harmonization and validation**

A district data harmonisation and validation meeting is recommended as a first step to ensuring data generated from the health facilities is a true account of what transpired during the quarter. Any inconsistencies should be rectified at this meeting.

Guidance on how to undertake this activity is as follows:

**i. Meeting time, venue and participants**

- The meeting should be held every quarter in the first week of the reporting month and should take a maximum of one day unless this is not possible in instances where there are many health facilities in the district.
- It should be held at district level and should include the following people: Health Facility TB Focal Person, Records Assistant/ Health Information Assistant, District TB/Leprosy Supervisor, Biostatistician/ HMIS Focal Person, Implementing Partner M&E/Data Officer

**ii. Meeting requirements**

- Participants from the Health Facilities should carry the following registers and reports: TB Laboratory Register, Presumptive TB Register, Unit TB Register, Leprosy Register, HMIS 106a Report draft.

**iii. Proceedings**

During the meeting the following should be done:

- Introducing the TB/Leprosy indicators and how to extract these from source registers/cards
- Trace and transfer of patients among facilities and complete documentation in registers with a focus on current cohort and cohort of the next quarter.
- Re-confirming and completing all patient treatment outcomes documented in registers as cured, completed, died, treatment failed, lost to follow-up by clarifying dates of last regimen pickup or clinic contact
- Re-counting patients recorded in registers with emphasis on Presumptive patients identified, PBCs recorded in the laboratory, patients registered in the Unit TB register, Rifampicin resistant cases identified and those transferred to 2nd Line treatment in the DR TB register
- Comparing what is recounted and what is reported in the hard copy HMIS 033b, HMIS 105 and HMIS 106a
- Comparing what is reported in the hard copy HMIS 033b, 105,106a with what is entered in DHIS2
- Correcting the confirmed numbers on hard copy reports
- Correcting what is entered in DHIS2
- Documenting sections that are under or over reported and conduct a root cause analysis for improvement in data quality.

## Roles and responsibilities

The NTLP M&E function incorporates activities like reporting and performance reviews, and it is important that roles and responsibilities at different levels are clearly defined.

*Table 56 Roles and responsibilities personnel*

Cadre	Roles and responsibilities
Health facility In charge	<ul style="list-style-type: none"> <li>● Coordinate compilation of quarterly HMIS 106a and TWOS reports, provide guidance and support to appropriate personnel to generate and compile these reports</li> <li>● Ensure accuracy, consistency, completeness, integrity, precision, and timeliness of the reports generated by the health facility</li> <li>● Ensure that staff have up-to-date reporting tools and respect the reporting schedules</li> <li>● Approve the quarterly HMIS106a report and TWOS report generated by the health centre</li> <li>● Maintain archives of all reports submitted and feedbacks provided</li> <li>● Provide feedback to staff regarding reporting issues</li> <li>● Use the reports to develop graphs, set targets and make decisions</li> </ul>
Health Unit TB clinical teams	<p>The team comprises the Health Unit In-Charge, clinicians, laboratory and records staff. The team should:</p> <ul style="list-style-type: none"> <li>● Ensure the relevant sections HMIS 106a etc and TWOS reports are complete, accurate, timely and consistent with the reporting requirements</li> <li>● Verify the accuracy, integrity and completeness of the data from all service delivery points including the laboratory before submitting to the Health Centre In-Charge</li> <li>● Compile a list of transfer in and transfer out patients</li> <li>● Carry out physical counts of available supplies in their stores</li> </ul>
District TB Leprosy Supervisors and other DHT members	<ul style="list-style-type: none"> <li>● The DTLS shall compile and keep a list of all the health facilities involved in the diagnosis and treatment of TB especially those accredited through the gazetted NTLP mechanisms</li> <li>● The DTLS shall always display an up-to-date list of DTUs at the district headquarters and share the same with the National TB and Leprosy Program data manager</li> <li>● On a quarterly basis (and with DHMT) provide training, support supervision, mentorship, coaching and on-job support to health facilities on TB management and reporting</li> <li>● Ensure all TB diagnostic, treatment &amp; TB diagnostic and treatment units including private facilities, standalone laboratories etc. submit their reports</li> <li>● Ensure the accuracy, consistency, completeness, integrity, precision, and timeliness of the reports (including HMIS 106a and TWOS) generated by the health facility before biostatistician enters them into DHIS2</li> <li>● Convene the district quarterly performance review meetings as agreed with the DHO and IPs</li> <li>● Provide summary to the DHO and DHMT on district and facility performance of key TB and leprosy indicators</li> </ul>
District Health Team (DHO)	<ul style="list-style-type: none"> <li>● The DHO with support should arrange, coordinate and conduct periodic/ quarterly data quality assessments</li> <li>● DHO should arrange for district review meetings to discuss the performance of the TB activities</li> <li>● DHO should ensure that TB and leprosy reports are accurate, complete and consistent and are submitted into DHIS2 in time</li> </ul>

## TB monitoring tools

Monitoring requires that there should be “monitoring tools” to support data capture and reporting. The NTLP uses the following forms and registers as tools to monitor program activities.

*Table 57 TB monitoring tools*

Level	Tools (Recording and/or reporting)	
National	TB performance assessment and mentorship tool	
District	District TB Register	TB performance assessment & mentorship tool
	Quarterly Report Forms (Case finding (notification form) and treatment outcome)	
Facility	OPD register	TB Patient Treatment Card
	ANC Register	TB Unit Register
	IPD Register	TB Preventive Therapy Register
	Maternity Register	Contact tracing register
	HTS Register	DR TB treatment patient consent form
	Presumptive TB Register	Second line TB treatment card
	Request for TB specimen examination	DR TB register
	TB laboratory request form	Patient referral and transfer form
	TB Laboratory Register	HMIS 033b, 105, 108 & 106A
	Culture and sensitivity request form	Quality Improvement Documentation Journal
Community	VHT/ICCM Register	Community sensitisation and screening form
	VHT referral form	Community TB follow up register
	Quarterly VHT ICCM summary	Community TB contact tracing form

Table 58 TB indicators

<b>Group</b>	<b>Definition/ Indicators</b>	<b>Levels</b>		
		<b>Facility</b>	<b>District</b>	<b>National</b>
Case finding	Measures detection of TB patients in the population, disaggregated by age			
TB Case detection rate		x	x	x
Proportion of TB cases notified		x	x	x
Proportion of TB cases notified from the private sector			x	x
TB Incidence rate		x	x	x
Proportion of childhood TB cases		x	x	x
Number of TB contacts identified		x	x	x
Proportion of people aware about TB signs and symptoms			x	x
Proportion of people with symptoms of TB from the community that seek care from health facilities			x	x
Proportion of TB patients facing stigma and discrimination				x
Proportion of PFPs reporting on TB screening in DHIS2 in the outpatient department			x	x
Proportion of PNFPs reporting on TB screening in DHIS2 in the outpatient department			x	x
Proportion of PFPs diagnostic and treatment units reporting DHIS2: HMIS 106a in DHIS2			x	x
Case holding	Measures how well TB patients adhere to the anti-TB drugs prescribed for them	<b>Facility</b>	<b>District</b>	<b>National</b>
Cure rate		x	x	x
Proportion of new TB cases successfully treated (cured plus treatment)		x	x	x
Proportion of TB patients diagnosed and not started on treatment (initial loss to follow up)		x	x	x
Treatment success rate for incident TB cases		x	x	x
Lost to follow up rate		x	x	x
TB mortality rate		x	x	x
Treatment failure rate		x	x	x
Program management	<b>Facility</b>	<b>District</b>	<b>National</b>	
TB catastrophic costs				x
Proportion of supervisory visits carried out			x	x
Proportion of TB treatment facilities reporting stock-outs of anti-TB drugs			x	x
National TB contact tracing coverage				x
National TB contact screening coverage				x
Proportion of TB patients on DOT		x	x	x
Completeness of reporting to NTLP		x		x
Accuracy of reporting to NTLP		x		x
Timeliness of reporting				x
Proportion of private health facilities reporting		x		
TB/HIV collaboration	These cover activities that are, or can be, conducted at a TB treatment health facility	<b>Facility</b>	<b>District</b>	<b>National</b>
Proportion of notified TB cases with a documented HIV status		x	x	x
Proportion of HIV testing among TB patients		x	x	x
Proportion of positive HIV tests among TB patients		x	x	x
Proportion of HIV-positive TB patients started or are receiving ART		x	x	x
Proportion of eligible PLHIV given TB preventive therapy		x	x	x
Proportion of new TB/HIV cases successfully treated (cured plus treatment completed)		x	x	x

(Continued overleaf)

Table 59 TB Indicators (continued...)

Group	Definition/ Indicators	Levels		
		Facility	District	National
TB in children				
Childhood TB treatment coverage		x	x	x
Proportion of all incident (new and relapse TB) cases notified to/by the program, who are children		x	x	x
Proportion of children <5 years who are contacts of TB patients on treatment that are screened for active TB		x	x	x
Proportion of eligible children <5 years who are contacts of people with TB, who are put on TPT		x	x	x
Proportion of other close contacts (>5 years) of people with TB who are put on TB preventive therapy		x	x	x
<i>Data source: Unit TB register, TPT register</i>				
Laboratory services		Facility	District	National
Proportion of notified new and relapse TB cases with bacteriological confirmation		x	x	x
Proportion of notified new and relapse TB patients diagnosed using WHO recommended rapid tests		x	x	x
Proportion of TB microscopy units submitting slides for rechecking				x
Proportion of TB presumptive patients who are sputum smear positive		x	x	x
Proportion of sputum smear-positive PTB registered for treatment		x	x	x
Proportion of public health facilities (HC III and HC IV) offering gene Xpert diagnostic services			x	x
Proportion of MDR-TB identified out of cultured specimen			x	x
Proportion of laboratories participating in EQA			x	x
Proportion of notified, bacteriologically confirmed TB cases with DST for rifampicin		x	x	x
<b>Programmatic Management of Drug Resistant TB</b>		Facility	District	National
Percentage of close contacts of DR-TB patients traced and screened for TB		x	x	x
Proportion of MDR TB cases detected that are linked to treatment		x	x	x
Proportion of Drug resistant TB cases successfully treated (cured plus treatment completed)		x	x	x
Death rate for confirmed DR-TB patients		x	x	x
Lost to follow up rate for confirmed DR-TB patients		x	x	x
Proportion of MDR TB cases detected		x	x	x
Proportion of MDR TB cases detected that are linked to treatment		x	x	x
Proportion of DR TB patients tested by whole gene sequencing		x	x	x
Percentage of notified, rifampicin-resistant TB cases with DST results for Fluoroquinolones		x	x	x

The indicators, calculation, data source, level and frequency of measuring the indicators should be indicated for each of the above categories are shown in the Tables that follow.

## Monitoring TB program performance

Table 60 TB case holding

No.	Indicator	Calculation	Data Source	Level				Frequency	
				Health facility	District	Region	Central	Quarterly	Annual
1	Cure rate among new PBC	Numerator: Number of new Pulmonary Bacteriologically Confirmed (PBC) TB patients with cured treatment outcome	Unit TB register, Quarterly reports on treatment outcomes	x	x		x	x	x
		Denominator: Total number of new Pulmonary bacteriologically confirmed (PBC) TB patients registered in that quarter							
2	Treatment success rate	Numerator: Number of new TB cases registered in the previous year that were successfully treated (cured plus treatment completed)	Unit TB register, Quarterly report on treatment outcomes	x	x		x	x	x
		Denominator: Total number of new TB cases notified to the national health system in the previous year							
3	Treatment success rate for incident TB cases	Numerator: Number of notified new and relapse TB patients who are cured plus those who completed treatment	Unit TB register, Quarterly report on treatment outcomes	x	x		x	x	x
		Denominator: All notified new and relapse TB patients in a given period							
4	TB mortality rate	Numerator: Estimated no. deaths due to TB	Unit TB register, Quarterly report on treatment outcomes, Country census	x	x		x	x	x
		Denominator: Country population based on UBOS or UN Population division							
5	Loss to follow up rate among PBC	Numerator: Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in a quarter that get lost to follow up	Unit TB register, Quarterly report on treatment outcomes	x	x		x	x	x
		Denominator: Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter							
6	Treatment failure rate among PBC	Numerator: Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in a quarter who remained sputum smear-positive 5 months or later after starting treatment	Unit TB register, Quarterly report on treatment outcomes	x	x		x	x	x
		Denominator: Total number of new Pulmonary bacteriologically confirmed (PBC) TB cases registered in that quarter							
7	Proportion of TB patients on DOT	Numerator: Total number of TB patients receiving treatment under DOT during a given quarter or year	Unit TB register, Quarterly report on case-finding and treatment outcomes		x		x	x	x
		Denominator: Total number of TB patients registered in the specified quarter/year							

Table 61 TB program management

TB program management								
No.	Indicator	Calculation	Data Source	Level			Frequency	
				Health facility	District	Region	Central	Quarterly
1	TB catastrophic costs	Numerator: Number of TB affected households facing catastrophic spending	Cost survey			x	x	x
		Denominator: Number of TB affected households				x		
2	Proportion of supervisory visits carried out	Numerator: Total number of supervisory support visits made in a quarter for region or district	Quarterly report on program management		x	x	x	x
		Denominator: Total number of planned supervisory support visits for region or district				x		
3	National TB contact tracing coverage	Numerator: Number of PBC TB registered patients whose contacts were traced	Quarterly report on program management		x	x	x	x
		Denominator: Total number of TB PBC registered cases				x		
4	Proportion of TB treatment Health facilities reporting stock-outs	Numerator: Total number of TB treatment health facilities that reported stock-out of TB medicines in each quarter or year	Reports on support supervision visits		x	x	x	x
		Denominator: Total number of TB treatment health facilities				x	x	
5	Completeness of reporting to NTLP	Numerator: Total number of districts that submitted TB case- finding and treatment outcomes report to NTLP in each quarter or year	Regional and NTLP reports			x	x	x
		Denominator: Number of districts expected to submit TB case- finding and treatment outcomes reports to NTLP in each quarter or year				x	x	x
6	Accuracy of reporting to NTLP	Numerator: Number of TB case-finding and treatment outcome reports submitted that were recorded completely and accurately	Regional Unit and district TB registers		x	x	x	x
		Denominator: Total number of case-finding and treatment outcome reports examined for completeness and accuracy				x	x	x

Table 62 Monitoring TB/ HIV collaboration

Monitoring TB/ HIV collaboration									
No.	Indicator	Calculation	Data Source	Level			Frequency		
				Health facility	District	Region	Central	Quarterly	Annual
1	Proportion of notified TB cases with a documented HIV status	Numerator: No. TB notified TB cases with a documented HIV status	TB unit and district registers, Quarterly report on case-finding	x	x		x	x	x
		Denominator: No. notified TB cases							
2	Proportion of TB patients who are HIV- positive	Numerator: Number of registered TB patients in a given quarter or year who tested HIV-positive	TB unit and district registers, Quarterly report on case-finding	x	x		x	x	x
		Denominator: Total number of TB patients registered in the same quarter and tested for HIV							
3	Proportion of new TB/HIV cases successfully treated (cured plus treatment completed)	Numerator. Number of new TB cases registered in the previous year that were successfully treated (cured plus treatment completed)	DHIS2: HMIS 106a	x	x		x	x	x
		Denominator. Total number of new TB cases notified to the national health system in the previous year							
4	Proportion of registered TB patients co- infected with HIV started or are receiving ART during TB treatment	Numerator: Number of registered TB patients in a given quarter co-infected with HIV who started or continued ART	TB unit/district registers, Quarterly reports on TB case-finding and treatment outcomes	x	x		x	x	x
		Denominator: Total number of registered TB patients in the same quarter co-infected with HIV							
5	Proportion of eligible PLHIV given TB preventive therapy	Numerator. Number of newly enrolled PLHIV given TB preventive Therapy	TPT register	x				x	
		Denominator. Total number of eligible PLHIV							

Table 63 Monitoring TB in children

Monitoring TB in children									
No.	Indicator	Calculation	Data Source	Level			Frequency		
				Health facility	District	Region	Central	Quarterly	Annual
1	Proportion of all incident (new and relapse TB) cases notified to/by the program, who are children	Numerator: Number of childhood TB cases (new and relapses)	Unit and district TB registers Quarterly report on program management	x	x	x	x	x	x
		Denominator: Total number of registered TB cases in the same quarter; number of all cases of all forms of TB (new and relapses)							
2	Proportion of eligible children under 5 years who are contacts of people with TB, who are put on TB preventive therapy	Numerator. eligible children under 5 years who are contacts of people with TB, who are put on TB preventive therapy	TPT Register	x	x	x	x	x	x
		Denominator. Total number of eligible children under 5 years who are contacts of people with TB							
3	Proportion of other close contacts (>5 years) of people with TB who are put on TB preventive therapy	Numerator. Number of other close contacts (>5 years) of people with TB who are put on TB preventive therapy	TPT Register	x	x	x	x	x	x
		Denominator. Total number of eligible close contacts (>5 years) of people with TB							

Table 64 Systematic screening and TPT indicators

Systematic screening and TPT									
No.	Indicator	Calculation	Data Source	Level			Frequency		
				Health facility	District	Region	Central	Quarterly	Annual
1	National TB contact tracing coverage	Numerator: Number of PBC TB registered patients whose contacts were traced	Contact tracing register	x	x	x	x	x	x
		Denominator: Total number of TB PBC registered cases							
2	Number of TB contacts identified	Numerator: Number of TB contacts screened for TB	Contact tracing register	x	x	x	x	x	x
		Denominator: Number of TB contacts identified							
3	TPT coverage (expressed as a percentage)	Numerator: Total number of individuals eligible for TPT who initiated treatment during the reporting period	TPT Register	x	x	x	x	x	x
		Denominator: Total number of individuals eligible for TPT during the reporting period							
4	TPT completion (expressed as a percentage)	Numerator: Total number of individuals who completed a course of TPT* during the reporting period	TPT Register	x	x	x	x	x	x
		Denominator: Total number of individuals who initiated a course of TPT during the reporting period							

Table 65 Monitoring TB laboratory services

TB laboratory services									
No.	Indicator	Calculation	Data Source	Level				Frequency	
				Health facility	District	Region	Central	Quarterly	Annual
1	Proportion of notified new and relapse TB cases with bacteriological confirmation	Numerator: Number of notified new and relapse TB cases with bacteriological confirmation	Laboratory and/or presumptive TB register	x	x		x	x	x
		Denominator: Total number of notified new and relapse TB cases							
2	Proportion of pulmonary bacteriologically confirmed PTB registered for treatment	Numerator: Number of new pulmonary bacteriologically confirmed TB patients who have initiated treatment during a quarter/year	Laboratory, Unit and District TB registers	x	x			x	x
		Denominator: Total number of new pulmonary bacteriologically confirmed TB patients detected in same quarter							
3	Proportion of MDR-TB identified out of cultured specimens	Numerator: Number of MDR-TB patients diagnosed in a quarter/ year	NTRL					x	x
		Denominator: Number of cultures performed in the same quarter/year							
4	Cumulative number of MDR-TB reported	Count Total number of MDR-TB patients diagnosed in a quarter/year	NTRL					x	x
5	Proportion of health facilities with high false negative AFB smear	Numerator: Number of health units sampled having at least two high false negative AFB smear microscopy results	NTRL					x	x
		Denominator: Total number of health units sampled							
6	Proportion of notified new and relapse TB patients diagnosed using WHO recommended rapid tests	Numerator. Number of public health facilities (HC III and HC IV) offering GeneXpert diagnostic services	NTRL					x	x
		Denominator. Total number of notified new and relapse TB patients tested with mWRD (e.g., GeneXpert) as initial diagnostic test							
7	Proportion of public health facilities (HC III and HC IV) offering GeneXpert diagnostic services	Numerator. Number of public health facilities (HC III and HC IV) offering GeneXpert diagnostic services	DHIS2: HMIS 105 (Lab section)					x	x
		Denominator. Number of public health facilities (HC III and HC IV)							
8	Proportion of laboratories participating in EQA (GeneXpert)	Numerator: Number of laboratories participating in EQA for GeneXpert	NTRL					x	x
		Denominator: Number of laboratories conducting GeneXpert testing							
9	Proportion of laboratories participating in EQA (microscopy)	Numerator: Number of laboratories participating in EQA for microscopy	NTRL					x	
		Denominator: Number of laboratories conducting sputum smear microscopy							
10	Proportion of notified, bacteriologically confirmed TB cases with DST for rifampicin	Numerator. Number of notified new and relapse bacteriologically confirmed TB cases with DST for rifampicin	DHIS2: HMIS 106a					x	x
		Denominator. Total number of notified new and relapse P-BCs							

Table 66 Programmatic Management of Drug Resistant TB indicators

Programmatic Management of Drug Resistant TB								
No.	Indicator	Calculation	Data Source	Level			Frequency	
				Health facility	District	Region	Central	Quarterly
1	Percentage of close contacts of DR-TB patients traced and screened for TB (at least once)	Numerator: Number of contacts of MDR TB cases screened for TB	Contact tracing register for susceptible and Resistant TB	x	x	Rx initiation site	x	x
		Denominator: Total number of contacts of MDR-TB patients						
2	Proportion of MDR TB cases detected	Numerator: Number of MDR patients notified	Laboratory register	x	x		x	x
		Denominator: Number of total expected MDR TB cases						
3	Proportion of MDR TB cases detected that are linked to treatment	Numerator: Number of laboratory-confirmed MDR-TB cases registered and started on a prescribed second-line anti-TB treatment regimen during the specified period of assessment	MDR Register	x	x		x	x
		Denominator: Number of laboratory-confirmed MDR-TB cases registered						
4	Proportion of Drug resistant TB cases successfully treated (cured plus treatment completed)	Numerator: Number of laboratory-confirmed MDR-TB patients enrolled on second-line anti-TB treatment during the year of assessment who are successfully treated (cured plus completed treatment)	MDR Register	x	x		x	x
		Denominator: Total number of confirmed MDR-TB patients enrolled on second-line anti-TB treatment during the year of assessment						

## CHAPTER 11: LEPROSY

### Definition of Leprosy

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* also known as Hansen bacillus, which produces a chronic systemic granulomatous disease that affects the skin, peripheral nerves and the mucous membranes. The disease affects people of all races and ages and both sexes.

A case of leprosy is a person with clinical signs of leprosy who requires chemotherapy (MDT). This excludes people with residual signs of leprosy after completion of a full course of treatment.

### Source of infection and mode of transmission

The mode of transmission is uncertain, but it is believed that *M. leprae* is spread from person to person primarily via droplets from the nose and mouth during close and frequent contact with untreated cases. Untreated leprosy patients discharging bacilli are considered the main source of infection. Persons living in the same household or who otherwise are in frequent contact with an infectious person have the greatest risk of being exposed to the bacilli.

The incubation period is usually long, ranging from 3 to 5 years but it may vary from 6 months to more than 20 years. The peak age of onset is young adulthood, usually 20 to 30 years of age. Whereas there are published reports of people co-infected with leprosy and HIV, there is no conclusive evidence suggesting an association between HIV infection and leprosy.

### Natural history

While most individuals exposed to an infectious case of leprosy become infected, only a very small proportion (less than 5 percent) of those infected develop the disease. In the majority of cases (95%), specific host immunological defences kill the bacilli. The incubation time is variable and could range from 6 months to 20 years. Leprosy is a highly variable disease, affecting different people in different ways, according to their immune response. At one end are patients with a high level of immunity and will harbour a low number of bacilli. These are referred to as patients with Pauci bacillary (PB) leprosy. At the other end are patients with low immunity that harbour many bacilli in the body. These are referred to as patients with Multibacillary (MB) leprosy. Patients with many leprosy bacilli are classified as Multibacillary (MB) leprosy. They are considered the main source of infection. Untreated multibacillary leprosy patients continue to spread the infection. When left untreated, leprosy can cause progressive and permanent damage to the skin, nerves and eyes.

## CASE FINDING AND DIAGNOSIS OF LEPROSY

A case of leprosy is a person presenting with clinical signs of leprosy who requires complete course of treatment (MDT).

Leprosy is diagnosed by finding at least one of the following cardinal signs:

- i. Hypo pigmented/ reddish skin patches with definite loss of sensation
- ii. Thickened or enlarged peripheral nerves, with loss of sensation and/or weakness of the muscles supplied by those nerves
- iii. The presence of acid-fast bacilli in a slit skin smear

## **Case definition**

Once a case of leprosy has been diagnosed, it's important to define it as follows:

- **Paucibacillary (PB) case:** a case of leprosy with 1 to 5 skin lesions, without demonstrated presence of bacilli in a skin smear.
- **Multibacillary (MB) case:** a case of leprosy with more than five skin lesions; or with nerve involvement (pure neuritis, or any number of skin lesions and neuritis); or with the demonstrated presence of bacilli in a slit-skin smear, irrespective of the number of skin lesions.

## **Case-finding**

- Early diagnosis and prompt treatment reduce disabilities due to leprosy and stops transmission to others
- Early detection of new patients is a joint effort of communities and health service providers
- Persons with suspected signs should be referred to the nearest diagnostic facility
- Leprosy is diagnosed after finding at least one of the three cardinal signs
- Leprosy patients are classified into PB and MB for purposes of determining the treatment regimen
- Newly diagnosed patients should receive sufficient explanation to ensure prompt and proper treatment

The NTLP aims at early diagnosis of most cases occurring in the community by:

- i. Training health workers to correctly identify leprosy signs and symptoms
- ii. Providing health education to communities aimed at increasing awareness of leprosy
- iii. Engaging Village Health Teams in leprosy case finding initiatives
- iv. Delivering good treatment services to known leprosy patients, so that people with suspected signs and symptoms may have confidence in the good treatment and thus come forward to be examined and treated (self-reporting)
- v. Establishing a clear referral system to deal with difficult diagnoses
- vi. Proper examination of all persons presenting themselves at health facilities with different skin conditions
- vii. Carrying out systematic examination of house-hold contacts of all newly detected leprosy cases
- viii. The contact examination should be done annually for at least five (5) years

## **When to suspect leprosy (only start treatment after confirmation by trained health worker)**

- i. Leprosy should be suspected in people with any of the following symptoms and signs:
- ii. Pale or reddish patches on the skin (the most common sign of leprosy)
- iii. Loss of sensation in the skin patch
- iv. Numbness or tingling of the hands or feet
- v. Weakness of the hands, feet or eyelids
- vi. Painful or tender nerves
- vii. Swellings or lumps in the face or earlobes
- viii. Painless wounds or burns on the hands or feet
- ix. Deformities which can be in the eyes, hands, feet and nose
- x. Nasal congestion, bleeding, etc.
- xi. Enlarged peripheral nerves

## **Steps to examine a person suspected to have leprosy**

- i. Discuss with the person about the examination procedure
- ii. Examine the suspected person in adequate day light.
- iii. Examine the whole skin from head to toe while guaranteeing the person's privacy
- iv. Test the skin patches for sensation
- v. Palpate the peripheral nerves
- vi. Examine eyes, hands and feet for nerve damage
- vii. Refer for confirmation of diagnosis if unable to diagnose

## **Leprosy Diagnosis**

Diagnosis of leprosy must be based on careful **history taking** and **clinical examination** of the patient and, when necessary, backed by **bacteriological examination** (slit skin smears or pathological examination of biopsies).

It is recommended that a physical examination be carried out with adequate natural light (preferably daylight) because it is difficult to see the lesions in poor light.

Leprosy is diagnosed when at least one of the following **cardinal signs** is present:

1. Hypo pigmented patches with definite loss of sensation
2. Thickened or enlarged peripheral nerves at sites where nerves are often affected (see Figure 20) with loss of sensation and/or weakness of the muscles supplied by those nerves
3. The presence of acid-fast bacilli in a slit skin smear

A patient not having at least one of those signs should NOT be registered as a case of leprosy

## **Diagnostic and treatment units for leprosy**

- One or more health facilities in every district will be designated as a diagnostic and treatment unit for leprosy. The number of such units will be determined according to the level of endemicity of leprosy in the district.
- Staff at diagnostic units will be expected to diagnose, register and treat leprosy patients as recommended.
- At undesignated facilities, specific treatment must be given only after the diagnosis has been confirmed by the District TB/Leprosy Supervisor (DTLS) or appropriate staff of the nearest leprosy diagnostic/treatment center. If the DTLS is not expected to visit the facility soon, the patient should be referred to the unit where the DTLS is based or to the nearest leprosy diagnostic and treatment unit.

## **Responsibilities of health workers in leprosy diagnostic and treatment units**

- i. Carry out a complete physical examination
- ii. Confirm the diagnosis of leprosy
- iii. Explain to the patient what the disease is, what might be expected of treatment and possible complications
- iv. Prescribe the appropriate treatment and inform the patient where and when the treatment can be accessed
- v. Enter the patient's particulars in the patient record card, and the Unit Leprosy Register. The unit in-charge should notify the patients through the HMIS
- vi. Write and issue out the patient's clinic appointment card
- vii. Carry out systematic assessment of the close contacts of the newly detected patient within the first one month of establishing the diagnosis.

NB: This should be done annually for at least five years.

## **Leprosy related responsibilities of the DTLS on visiting a health unit**

The DTLS or other designated Focal Person on visiting a health facility does the following:

- i. Carries out complete physical examination on known leprosy patients and those with symptoms and signs suggestive of leprosy
- ii. Validates the information recorded by the health facility staff on the Leprosy Record Card and the Unit Leprosy register
- iii. Organizes the taking of skin smears when necessary
- iv. Explains to the patient about the disease and its treatment
- v. Enters patient data in the District Leprosy Register
- vi. Enters the District Registration number in the Unit Leprosy Register, Leprosy patient Record Card
- vii. The DTLS fills the discharge certificate for those that have completed treatment

## **Clinical examination**

Information that must be asked for and recorded on the Leprosy Record Card:

- General information on the patient: complete name, sex, date of birth, full address (village, Parish and sub-county), mobile telephone number, distance from home to health unit, occupation
- Contact information: Other people in the same household and family (including children) and indicating if any of them were ever diagnosed or treated for leprosy.
- History taking
- Main complaints: date of onset, sites of the lesions, subsequent changes and development of the disease, treatment received
- Physical examination
- It is recommended that the physical examination be carried out with:
  - adequate light available, because it is difficult to see the lesions in poor light
  - enough privacy for the person to feel at ease

To ensure that no important sign is missed, the clinical examination should include the entire skin surface, back and front in the following sequence:

- i. Head and neck
- ii. Front of chest and abdomen
- iii. Arms
- iv. Back of chest and buttocks
- v. External genitalia in male patients
- vi. Legs

### **Examination of the skin**

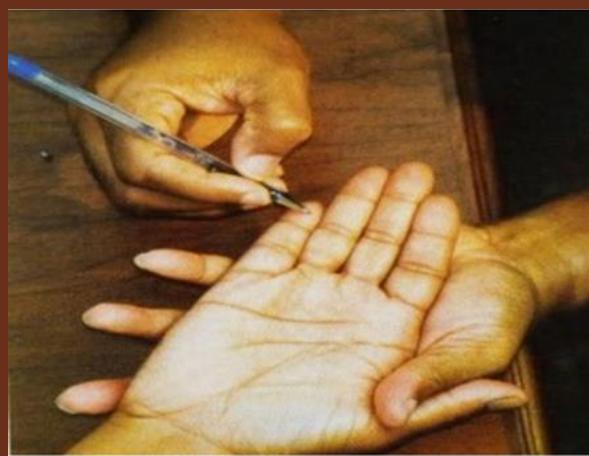
The skin should be examined for:

- i. Presence of skin lesions (patches, nodules, infiltrative skin changes, papules or plaques)
- ii. Number of skin lesions
- iii. Loss of sensation on the skin lesions (patches)

*Figure 30 Instructions for sensory testing*

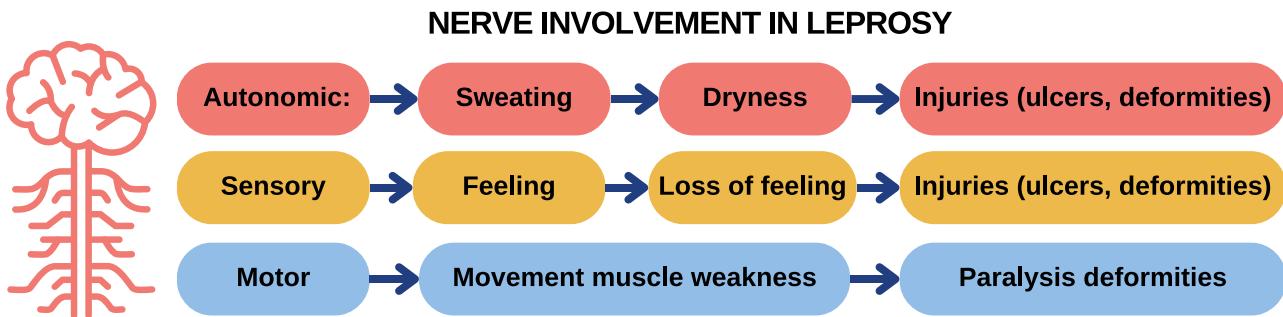
#### **Test the sensation of skin lesions with a wisp of cotton wool as follows:**

1. Roll the end of a wisp of cotton wool into a fine point.
2. A female HW should examine a female client or in the presence of a woman (chaperone)
3. Explain to patient the purpose of the test to obtain consent.
4. After the explanation, conduct a trial test by touching the patient on normal skin with his/her eyes open so that he/she can exactly see what is done. Continue until the patient shows that he/she understands the purpose of the test
5. Then do the testing with the patient's eyes closed. First test on normal skin. When the patient points correctly, test in the skin patches while touching normal skin now and then watch at every touch that the patient keeps his/her eyes closed
6. Touch the skin with this point so that the cotton wool bends
7. The patient should be asked to indicate accurately with the tip of a finger, every spot you have touched with the cotton wool



Sometimes patients point accurately to areas of normal skin but point more than 2cm away from where the skin patch is tested. This is called mis-reference, and shows diminished sensation in the patch. If this is consistent during repeated testing of a patch, it is a cardinal sign and thus diagnosis of leprosy is made. For thickened skin areas such as the palms and soles use the tip of a ballpoint pen for testing sensation

Figure 31 Nerve involvement in Leprosy

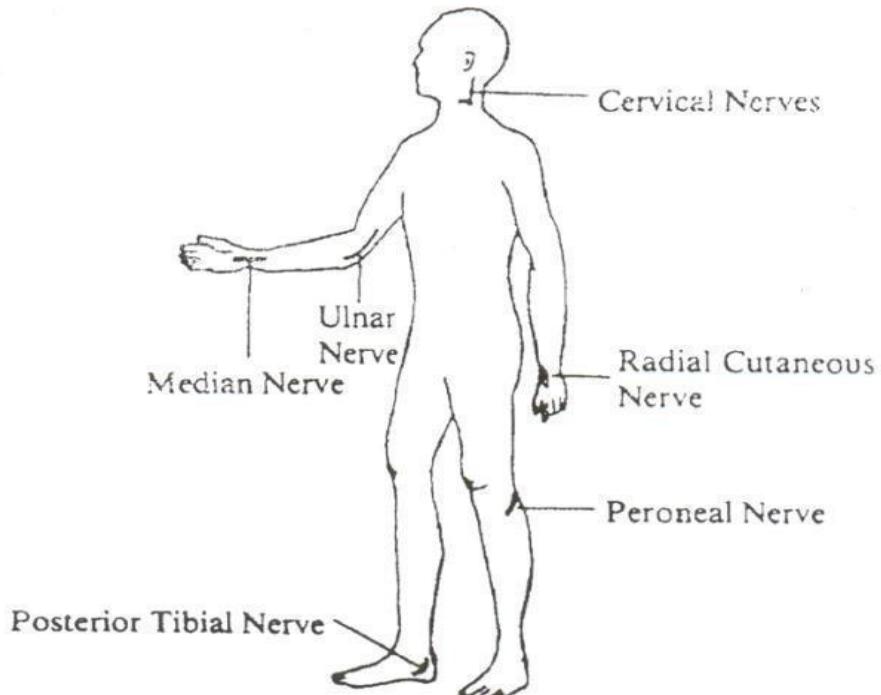


### Examination of peripheral nerves

The peripheral nerves are examined for:

- Size (enlargement or thickening)
- Tenderness (pain on palpation)
- Nerve function

Figure 32 Names of peripheral nerve trunks and sites where they can be palpated



### How to palpate nerves for size and tenderness

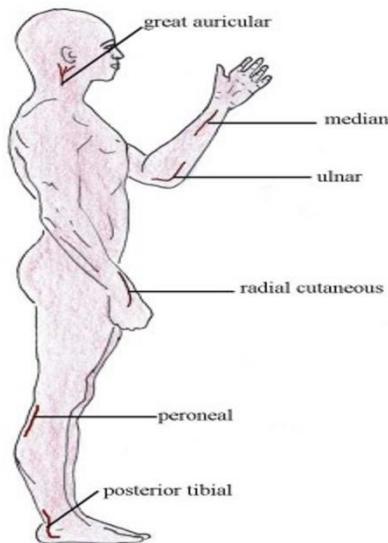
- To assess the thickness of a nerve, compare the size of your nerve to that of the patient
- Always compare the patient's left side with the right-side nerve(s)
- Palpate the nerve with 2 or 3 fingers by rolling the nerve on the surface of the underlying bone and determine the thickness and tenderness (pain on pressure) at the sites indicated in Figure 32 above
- Finding thick nerves, especially in combination with other signs and symptoms of leprosy, is diagnostic of leprosy

## How to carry out nerve function assessment

Peripheral nerve trunks carry 3 types of nerve fibres – **autonomic, sensory and motor**.

It is recommended to assess each nerve function separately. Any loss of function will indicate possible damage to the relevant nerve fibres. The most commonly affected nerves are: Ulnar, Median, Radial, Cervical, Posterior Tibial and peroneal nerves.

Figure 33 Nerves commonly affected by Leprosy



- **Autonomic nerve function** is assessed by looking for dry skin especially on the palms of the hands or the soles of the feet. Finding dry palms and soles of feet implies loss of autonomic nerve function.

- **Sensory nerve function** is assessed by carrying out sensory testing (ST) of the eyes, hands and feet as follows:

- **Eyes:** Observe the eyelids for blinking. If the patient is blinking, assume that the corneal sensation is normal. If the patient does not blink, record on the leprosy record card, "spontaneous blink absent" and refer the patient to the eye clinic.

- **Hands and feet:** Sensory testing on palms and soles should be done with a ballpoint pen on 10 standard points as indicated on the Leprosy Record Card. The procedure for sensory testing is described in Figure 35 below.

Figure 35 Procedure for sensory testing (ST) of hands and feet

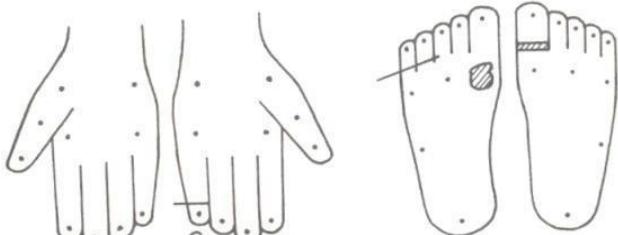
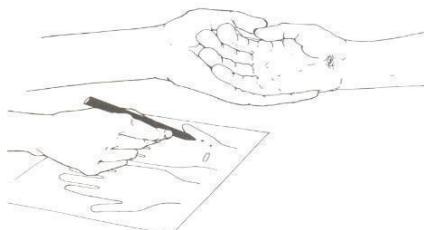


Figure 34 Marking the Leprosy card



Mark any wounds, open cracks, clawing of digits and bone loss or absorption on the Leprosy Record Card and support the patient's hand or foot to prevent any joint movements in fingers/toes during the test (Figure 34).

Figure 36 Sensory nerve testing



Then touch the skin very gently, denting it as little as possible, about 1 mm. The dots on the hand and foot maps on the Leprosy Record Card show you where to touch. First test while the patients is watching and ask them to point with one finger wherever they feel a touch, to the exact place touched. When patients understand the test well and are pointing clearly, ask someone to screen off their eyes or ask them to close their eyes and turn the face away.

Each time that you dent the skin, record on the hand or foot map on the Patient Record Card. Record ✓ (tick) at the place if the patient feels or points within 3 cm and X if they do not feel anything or point somewhere else.

**Motor nerve function:** The motor function of peripheral nerves is assessed through voluntary muscle testing (VMT). All muscle movements should be assessed for range and the strength against the resistance of your hand. Muscle strength should be graded as Strong (S), Weak (W) or Paralyzed (P). Test the muscle strength of eyes, hands and feet as follows:

### Procedure for Voluntary muscle testing (VMT) of eye



#### **Eye closure: [Facial nerve function]**

Ask patients to close their eyes lightly as in sleep. Observe whether or not the closure is complete. Inability to fully close the eye means the facial nerve has been affected, this is termed lagophthalmos.

If there is lagophthalmos, measure the lid gap. The lid gap is recorded in millimetres. A lid gap of more than 5 mm necessitates immediate action to prevent damage.

If closure is normal, record "0 mm". Then ask patients to close their eyes firmly while you gently check for strength.

Is the closure S, W or P?



#### **Procedure for VMT of hands and feet**

##### i. **Little finger out: [Ulnar nerve function]**

Ask patients to move their little finger all the way in (touching the side of the ring finger) and all the way out. Is the movement full?

If the movement is full, ask patients to hold their little finger out fully while you apply resistance to the outward movement at the base of the finger by pushing it in. Record the findings as S, W or P.

##### ii. **Thumb up: [Median nerve function]**



Ask patients to bring the thumb up and in front of the index finger but as far away from it as possible. Focus attention on the movements at the base of the thumb rather than the tip. Can they achieve this testing position? Is the movement full?

To test the strength of this movement, instruct patients to maintain the starting position while you push downwards towards the index finger. Record the findings as S, W or P

### iii. Wrist up: (Radial nerve testing)



The wrist should be supported by the examiners hand, with palm facing down and fingers in a light fist.

Ask the patient to take the wrist up and back as far as possible. If it can be moved full range, then resistance should be given on the back of the hand, pushing the hand down.



### iv. Foot up; [Peroneal nerve function]

Ask patients to fully lift their foot up towards the shin (dorsiflexion). Check if the movement is full (no more movement possible at the ankle joint).

To test the strength in the testing position, apply resistance to the top of the foot by pushing down.

Record the findings as S, W or P.

### v. Examination of other organs

Examination of other organs is important in cases of MB leprosy.

#### Examination of the eye

The eyes should be examined carefully under good light, preferably daylight. Besides the changes examined under VMT above, other aspects to be checked include:

Figure 37 Vision testing in Leprosy

1. Loss of eyebrows
2. Corneas for clearness, ulcers or scars
3. Conjunctiva for redness indicating infection, such as conjunctivitis (peripheral redness) or iridocyclitis (redness around the cornea)
4. Pupils for regular and round shape. Also check reaction to light and look for signs of cataracts
5. Eyeball pressure for glaucoma
6. Vision by asking the patient to count fingers



Vision testing (see Figure 37 above)

Stand 6 meters from the patient. The vision of each eye is tested separately. Ask the patient to cover one eye. Raise your hand against a light background and show the patient 4 times, different numbers of fingers and ask the patient to count aloud. If he can count fingers at 6 meters, record 6/60 for that eye. Then test the other eye.

A patient who cannot count fingers at 6 meters has severe visual impairment.

### **Examination of the nose, tongue and gums, throat, breasts and testes**

These organs can also be affected. They should be examined and, in case of doubt, the patients should be referred to leprosy referral centres

### **Diagnosis of leprosy**

**Diagnosis of leprosy thus can be made by the clinical signs alone.**

**However, in absence of definitive cardinal features, confirmation of leprosy can be done using slit skin smear microscopy using modified ZN stain for *Mycobacterium leprae* .**

Leprosy is diagnosed by finding at least one of the following cardinal signs:

1. Definite loss of sensation in a pale (hypopigmented) 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. Microscopic detection of bacilli in a slit-skin smear.

#### **vi. Examination of the skin smear**

A Slit skin smear is a test in which a sample of material is collected from a tiny cut in the skin and stained for *Mycobacterium leprae*. The purpose of taking a skin smear is usually to:

- Confirm the diagnosis of skin smear-positive MB leprosy in a suspect
- Help to diagnose MB relapse in a patient who has been previously treated
- Help with the classification of new patients

Only 1 slide, with smears taken from 2 sites must be collected and examined. The basic field guidelines for selection of skin smear sites and steps for taking skin smears are included in Annex 7. The technique for collecting and examining skin smears is described in the ILEP Learning Guide Three: How to do a skin smear for leprosy.

Skin smear services are available in the National TB Reference Laboratory (NTRL), Lira Regional Referral Hospital, and Buluba, Kagando, Kuluva and Kumi hospitals.

**One positive smear result is diagnostic for MB leprosy.**

## vii. Molecular diagnosis of leprosy using PCR

Polymerase Chain Reaction (PCR) is a molecular biology technique widely used for diagnosing and management of leprosy. PCR can detect *M. leprae* DNA in clinical samples, aiding in the early diagnosis of leprosy, especially in cases with atypical presentations or in skin smear-negative patients. PCR can also be used to monitor treatment effectiveness by detecting the presence of the bacterium over time.

PCR is highly sensitive and can detect low levels of bacterial DNA, which is crucial in early stages of the disease. PCR can provide results more quickly than traditional culture methods.

Limitations involve cross-reactivity with other mycobacteria which leads to false positives, and sensitivity may be lower in patients with certain forms of leprosy. And, PCR requires specialized laboratory facilities and trained personnel, which may not be available in all regions.

## viii. Main messages

### When the diagnosis of leprosy is certain:

- Carefully record all information on skin, nerves, hands, feet and other organs on the Leprosy record card
- Fill in all of the information asked for at the start of treatment as baseline information
- After each review examination, record every change in findings on the same card.

### If leprosy is suspected/presumed but the diagnosis is not certain:

- Patients should be labelled as "presumed"
- Educate them about symptoms and signs of leprosy and either:
- Refer to the nearest leprosy treatment unit or specialised leprosy management centre
- Consult the DTLS +/- the RTLS
- Consider the possibility of another skin disease and treat appropriately; or
- Wait three months and review the skin lesions again.

If it is leprosy, loss of sensation may now be observed. If there is no loss of sensation in the skin lesions and no enlarged nerves, but there are suspicious signs such as nodules or swellings on the face or earlobes, or infiltration of the skin, it is important to try and get a skin smear examination done. A positive skin smear confirms the diagnosis of leprosy while a negative result (in the absence of other cardinal sign) would rule out leprosy.

Figure 38 Cardinal signs for the diagnosis of Leprosy

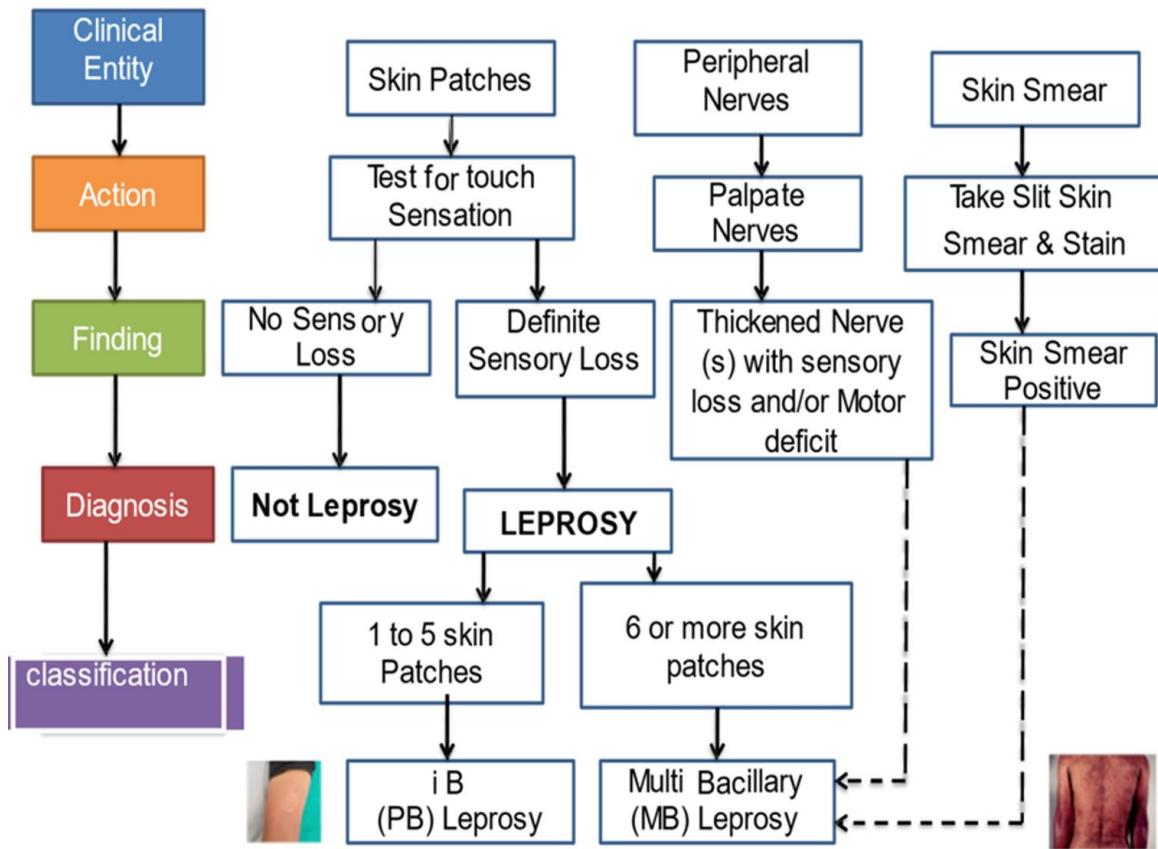
LEPROSY DIAGNOSIS IS CONFIRMED WHEN AT LEAST ONE OF THE CARDINAL SIGNS ARE PRESENT



Definite loss of sensation in a hypopigmented or reddish skin patch	Thickened Peripheral Nerve and with loss of sensation in the area supplied by that nerve, and/or weakness of the muscle supplied by that nerve	Presence of acid-fast bacilli in a slit skin smear
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Figure 39 Leprosy diagnosis and classification

## LEPROSY DIAGNOSIS AND CLASSIFICATION



### Classification of Leprosy

Classifying leprosy is essential for determining the treatment regimen and providing the right patient education. There are two treatment groups:

- Paucibacillary (PB) leprosy:** These are patients who have up to five skin lesions in total. These patients should also be skin smear-negative. This group of patients is likely to have high body resistance to leprosy bacilli.
- Multibacillary (MB) leprosy:** These patients have more than five skin lesions. All leprosy patients with a positive skin smear must be classified as MB, irrespective of the number of skin lesions. The bacilli infecting an individual with very low body resistance will multiply freely in the body, and the person will develop MB leprosy, the more severe form of the disease.

If there is doubt about the classification, the patient should be classified and treated as MB leprosy

## Differential diagnosis of leprosy

Leprosy can be easily mistaken for a number of skin diseases. If patients are examined carefully, mistakes in diagnosis should not occur as none of the cardinal signs of leprosy are found in the common skin diseases such as:

- **Birthmarks:** Lightly or deeply pigmented areas of different sizes that have been present since birth or soon after birth and do not change.
- **Post-inflammatory hypopigmentation:** The skin may become temporarily or permanently hypopigmented at the end of treatment of several inflammatory skin conditions. It also can follow the deliberate application of skin-lightening products for cosmetic reasons. This can be ruled out through appropriate history taking.
- **Tinea versicolor:** These lesions often itch. They are hypopigmented, but with no loss of sensation. Usually, they clear up within six weeks with application of antifungal ointment or cream.
- **Tinea corporis (ringworm):** Lesions are well-defined areas of hypopigmentation with white scales and without loss of sensation. Usually, they clear within six weeks of application of antifungal ointment.
- **Vitiligo:** a chronic skin condition characterized by portions of the skin losing their pigment causing whitish patches of different sizes and shapes often with no clear cause.
- **Pityriasis alba:** Present most commonly on the face, but the upper trunk may be affected. Hypopigmented rounded or oval patches, variable in size and with the margin sharply demarcated, covered with fine adherent scales. Often patients only present with the final hypopigmentation.
- **Psoriasis:** Raised areas with white fatty scales that bleed easily on scratching (test for pin point bleeding).
- Molluscum contagiosum: Nodular lesions with a depression in the center. Firm squeezing results in the appearance of a creamy substance.
- **Onchocerciasis** (in endemic areas): Previous complaints of intense itching. There are itchy nodules and scratch marks. Hypopigmented macules may be one of the manifestations. There is loss of sensation. In a later stage, there are mottled lesions particularly on the loins and shins. Skin smears are negative for AFB.
- **Neurofibromatosis:** Multiple deeply pigmented soft nodules that do not itch. Skin smears are negative for AFB.
- **Syphilis:** Secondary syphilis presents with a considerable variety of lesions, e.g., papular and nodular lesions. Skin smears are negative for AFB. Serological tests for syphilis will be positive.
- **Kaposi sarcoma:** In HIV-positive patients and others, Kaposi's sarcoma often presents with nodules on the face and ear lobes. There are often lesions within the mouth and the throat, which may bleed. Skin smears are negative for AFB.

## **Information to give patients diagnosed with Leprosy**

When patients are newly diagnosed with leprosy, they should receive help and counselling so that the disease can be treated quickly and in the best possible way. The following categories of messages should be given to patients (not necessarily at the same sitting):

### **1. General information**

- People affected by leprosy should continue to live a normal life
- Leprosy is caused by a germ and is curable
- Explain where to get answers to any questions regarding leprosy
- Consultation and treatment are free of charge
- Discuss how frequently the person should attend the clinic
- Persons who have been in close contact with patients, particularly those living in the same household, need to be examined at the earliest opportunity

### **2. Information about treatment**

- Leprosy is curable
- Leprosy is no longer infectious once treatment has begun
- The treatment lasts 6-12 months depending on the leprosy type
- Tablets must be taken every day at home
- A new blister pack is needed every 28 days
- Common side-effects include reddening of the urine and darkening of the skin
- The skin patches may take time to disappear

### **3. Information about Prevention**

- Contacts of Leprosy patients can be given preventive medicine e.g. Single Dose Rifampicin
- BCG given at birth can prevent one from getting Leprosy
- Any Skin lesion can be due to Leprosy, hence the need to seek medical attention

Complications called "reactions" may occur and can be treated. These can present as patches that suddenly become red, swollen, and more visible. There may be:

- Pain or numbness in the limbs
- Weakness of the hands or feet
- Swelling of hands and feet
- Eye problems such as redness, pain, or impairment of vision

### **Disabilities**

- New disabilities can occur at any time, but they can be managed
- Existing disabilities may or may not improve with treatment
- When problems occur, treatment may be available locally, or the patient may have to be referred to another clinic for specialist care
- Various new skills will have to be learnt to prevent and manage disability

## TREATMENT OF LEPROSY

The aims of leprosy treatment are to:

1. Cure the leprosy
2. Prevent the occurrence of disabilities
3. Prevent relapse and the development of drug-resistant leprosy

- MDT is a safe and effective oral treatment of leprosy
- It is provided as 28-day blister packs
- The intake of the monthly treatment containing rifampicin should be supervised
- There are different blister packs by age category for PB and MB leprosy patients
- The total duration of treatment is six months for PB leprosy and 12 months for MB leprosy
- Relapses after MDT are very rare

Patient centred care approach should be used to provide care and treatment to Leprosy patients. Facility and community differentiated service delivery models can be used where possible Multi month Drug dispensing should be practiced. (For Details refer to the TB/Leprosy DSD Guidelines)

### Multidrug Therapy

MDT is a combination of drugs that is very safe and effective in treating leprosy to prevent the emergence of drug resistance. Leprosy patients should never be treated with a single drug. The guidelines recommend a 3-drug regimen of rifampicin, Dapsone and clofazimine for all leprosy patients, with a duration of treatment of 6 months for PB leprosy and 12 months for MB leprosy.

This represents a change from the previous standard treatment for PB leprosy, which is rifampicin and Dapsone for 6 months, due to some evidence indicating better clinical outcomes with a 3-drug, 6-month regimen over a 2-drug, 6-month regimen. A potential advantage of using the same three drugs for PB and MB leprosy is simplification of treatment (i.e., the same blister pack could be used for treating both types of leprosy) and reduced impact of misclassification of MB leprosy as PB leprosy, since all patients will receive a 3-drug regimen.

Note:

- MDT is distributed free of charge to all those who need it
- The drugs are all taken orally. The daily drugs should be taken in a single dose on an empty stomach
- The drugs are given out in blister packs that provide four weeks of treatment (1 month)
- There are different packs with the same drugs but in smaller doses for children
- MDT is safe for women and their babies during pregnancy and breastfeeding
- MDT can be given to HIV-positive patients, those on antiretroviral treatment, and to patients on treatment for TB. If a leprosy patient is on treatment for TB, the MDT regimen should omit rifampicin as long as the TB regimen contains rifampicin

## MDT regimens

The standard adult treatment regimen for PB and MB leprosy is:

- Rifampicin:** 600 mg once a month
- Clofazimine:** 300 mg once a month and 50 mg daily
- Dapsone:** 100 mg daily

### Duration:

- 12 months (12 blister packs) for MB
- 6 months (6 blister packs) For PB

Figure 40 adult MDT blister pack (front and back)

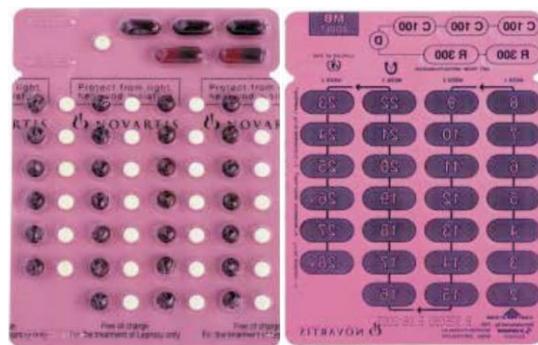


Figure 41 Child (10-14 years) MDT blister pack (front and back views)



Table 67 Recommended treatment (drugs and their doses)

Age	Drug	Dosage and frequency	Duration	
			PB	MB
Adult	Rifampicin	600 mg once a month	6 months	12 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	6 months	12 months
	Clofazimine	150 mg once a month, 50 mg daily		
	Dapsone	50 mg daily		
Children <10 years old or <40 kg	Rifampicin	10 mg/kg once month	6 months	12 months
	Clofazimine	6 mg/kg once a month and 1 mg/kg daily		
	Dapsone	2 mg/kg daily		

Note: The treatment for children with body weight below 40 kg requires single formulation medications since no MDT combination blister packs are available.

Every effort must be taken to ensure regularity of drug intake, so that PB patients complete their treatment in six months and MB cases in 12 months.

Specific blister packs are available for adults and children. The health worker or other accompanying person (if the health worker is not available) should ensure the patient take the monthly dose of treatment. This helps to guarantee that the treatment is taken properly as a measure to prevent drug resistance. It also gives the health worker an opportunity to check the patient for any complications of leprosy.

- The drugs administered once a month should be directly observed, the health worker should make sure that the drugs have actually been swallowed.
- The taking of the supervised dose is most conveniently arranged by having the patient attend the clinic each month. This monthly visit is also useful for monitoring the regularity of treatment and for identifying complications at an early stage. The other drugs are taken at home.

#### Accompanied MDT

1. If the patient is unable to visit the health centre regularly, provide enough blister packs that should last till the next visit
2. Give the first dose in the health centre and explain the monthly and daily doses
3. Fill out the patient's card
4. Make sure that every patient and accompanied person understand the treatment, how to take the drugs, well as side effects
5. Reassure the patients that they can live normal lives
6. Ask the patients to return after their treatment is complete

#### **MDT for children under 10 years of age**

The appropriate dose for children under 10 years of age can be decided on the basis of body weight. [Rifampicin: 10mg/kg body weight; clofazimine: 1 mg/kg body weight daily and 6 mg/kg body weight monthly; Dapsone: 2mg/kg body weight daily]. See table 61 above for guidance on dosing.

The standard child blister pack may be broken up so that the appropriate dose is given to children under 10 years of age. Clofazimine can be spaced out as required in consultation with the DTLS.

#### **MDT for MB patients with a very high bacterial index**

Rarely, it may be considered advisable to treat a patient with an average bacterial index (BI) of four or more for more than 12 months. This decision may only be taken by the Regional TB/Leprosy Focal Person or specialists at referral units, after careful consideration of the clinical and bacteriological evidence.

#### **MDT for leprosy patients who are co-infected with HIV**

For any leprosy patients who are co-infected with HIV and are receiving **Cotrimoxazole** preventive treatment (CPT), Dapsone should be stopped. In PB patients, Clofazimine and Rifampicin for the six months in the same dosage as used in the standard MDT. For MB patients, no further modification of the MDT regimen is required.

#### **Procedure for administering MDT**

- For patients to be treated with MDT, carry out the following steps:
- Determine which type of MDT is required, PB or MB determine which classification of leprosy because the new recommendation is to use the same drugs. The only difference is the duration: MB 12 months and PB 6 months).
- Fill in the Patient Record Card, the Leprosy Unit Register and the Patient's Identity Card.
- Counsel the patient (and the caregiver, if patient is a child).
- Directly observe first dose of treatment at initiation and explain how to continue the treatment at home.
- MDT is safe, and serious side-effects are very rare. Common side-effects are summarized in Table 68.

Table 68 Side-effects of MDT drugs and their management

Side-effects of MDT	Drug responsible	Management
Red urine	Rifampicin	Reassurance
Darkening of the skin	Clofazimine	Counselling
Gastrointestinal irritation e.g., abdominal pain, diarrhoea, nausea	All 3 drugs. Increased with high-dose clofazimine	Give drugs with food
Anaemia	Dapsone	Give iron and folic acid
Itchy skin rash	Dapsone	Stop dapsone and refer
Allergy, urticaria	Dapsone or rifampicin	Stop both and refer
Jaundice	Rifampicin	Stop rifampicin and refer
Shock, purpura, renal failure	Rifampicin	Stop rifampicin and refer

Note: Other drugs e.g. Minocycline, Ofloxacin and Moxifloxacin can be used if one or more of the standard drugs have been stopped, however, the determination of appropriate regimens and supervision of treatment should be undertaken by specialists.

### Ensuring treatment is taken regularly

- Patients should be treated with respect.
- Take time to explain the illness and its treatment to each patient.
- Make sure patients understand how to take the treatment and the date of their next clinic visit.
- Make sure there is a good supply of medicines ready for your patients to take.
- Listen to patients' concerns and answer their questions.
- With the consent of the patient, identify and engage another person (family member or other) as treatment supporter.
- Record the treatment given on the Patient's Identity Card, the Leprosy Record Card, and the Unit Leprosy Register.
- The DTLS should check those documents regularly to make sure that all patients are taking their treatment regularly.

### Management of patients who miss scheduled clinic visits

As soon as a patient misses an MDT appointment, action should be taken by the treatment facility staff to find out the reason and to remind him/her to attend the clinic regularly. This is facilitated by recording mobile telephone number for patient at the start of treatment. If this proves insufficient, a home visit by community health worker should be arranged (preferably within the first month following the date of the missed visit).

If patients have difficulty attending the clinic, it is possible to give them two blister packs at once, but in such cases, a treatment supporter (community volunteer, family member, or neighbour) should be involved in helping the patients to continue the treatment at home and reporting to the clinic in case of any problem.

- Patients may miss scheduled clinic visits for reasons such as:
- Poor accessibility of the clinic (long distance, difficult terrain, or inconvenient timing)
- Difficulty in getting time off at work
- Being overwhelmed with demands or effects of other health problems
- Nomadic life style
- Lack of understanding of the disease and the need for regular treatment
- Stigma
- Poor relationship with the health worker

## Treatment of leprosy in special conditions

- **Pregnancy and breast-feeding:** The standard MDT regimens are safe, both for the mother, the unborn child and the child and therefore can be administered during pregnancy and breast-feeding.
- **Patients co-infected with HIV:** Patients infected with HIV usually respond equally well to leprosy treatment as those without HIV infection.
- **Patients co-infected with TB:** Patients suffering from both TB and leprosy require standard TB treatment in addition to the standard MDT. Hence, skip the monthly dose of the rifampicin in the leprosy MDT regimen. Once the TB treatment is completed, the patient should continue his/her MDT, or the other way round

## How to care for patient at follow up visits

Every time patients come to take their drugs they should:

- Be asked if there have been any problems since the last visit
- Be re-examined including carrying out nerve function assessment
- Have the attendance recorded in the patient's card and the unit leprosy register
- Be informed about the remaining MDT doses and the date of their next visit
- Have the date of the next clinic visit recorded in the patients' identity card

## Management of patients who have completed MDT

When the patient has completed six months of treatment for PB leprosy or 12 months for MB leprosy, document in the unit register that the patient has completed the treatment under the heading "Treatment Outcome." Record any residual signs in the patient's record card and issue certificate for treatment completion.

Although patients who have completed MDT are cured, some signs of leprosy may remain:

- Skin patches caused by leprosy may not disappear immediately or may remain permanently.
- Loss of feeling, muscle weakness, and other nerve damage may also remain.
- These residual signs should be recorded on the Leprosy Record Card at the time of stopping MDT.

The patient should be counselled and asked to return to the clinic for review at least once a year or at any time when any of the previous symptoms recur. The patient should be counselled on the following issues:

- Significance of the remaining patches
- Essential actions to take in order to prevent further damage
- Signs and symptoms of reactions that can occur after MDT

**When patients return with a leprosy reaction after completing a full dose of MDT, only the reaction should be treated. This is not a reason to re-start MDT.**

## **Loss to follow up**

Every effort must be made to ensure that PB patients complete their treatment in six months and MB patients in 12 months. When that is not possible, the treatment regimen for PB leprosy must be completed within a maximum period of nine months. The treatment regimen for MB leprosy must be completed within a maximum period of 18 months.

Whenever a PB patient has missed more than three months of treatment, or an MB patient has missed more than six months, it is not possible for them to complete the regimen in the maximum time allowed, and they should be declared lost to follow up. This should be indicated in the Unit Leprosy Register under the heading "Treatment Outcome."

**A patient who fails to complete treatment within the maximum allowed timeframe is regarded as lost to follow up.**

Patients returning after loss to follow up should be examined and the findings recorded in the same way as for new cases. Returning patients should be managed as follows:

- Count the number of lesions to confirm the original classification
- Reclassify as PB or MB according to the number of lesions, register the patient under category "Treatment after Default" and treat with a full course of MDT
- If there are signs of reaction, manage appropriately
- Remember that a reaction can be mistaken for a return of the disease
- A patient who either remains very irregular on treatment or is repeatedly lost to follow up should be referred to specialized treatment centres for further management.

### **Reasons for referral for specialised care:**

The patient requires referral to an experienced physician or hospital if s/he has:

1. Severe reaction not responding to steroid treatment for 2 or 4 weeks (respectively for PB patients and MB patients)
2. Recurrent/chronic reaction
3. Red and/or painful eye
4. Diabetes
5. Not improved with current treatment
6. Developed a reaction for the second time
7. Deep ulcer(s)
8. Permanent paralysis that is suitable for reconstructive surgery

## **Relapse**

Relapse in leprosy is defined as the re-occurrence of the disease at any time after the completion of a full course of treatment with WHO-recommended MDT. Relapse after MDT is rare. It is important to continue vigilance because some sporadic cases of relapse due to drug resistance have been reported.

### **Signs of a relapse**

- The appearance of definite new lesions
- An increase in the skin smear BI of two or more units at any single site compared to BI taken from the same site at the previous examination. Care should be taken to exclude patients suffering from leprosy reactions
- MB patients who start MDT with an average BI of four or more are more likely to suffer a relapse later; most relapses occur long after the treatment was given (sometimes more than 10 years later)

It can be difficult to distinguish relapses from reactions. Table 69 provides guidelines for distinguishing relapses from reactions.

*Table 69 Differentiating a leprosy relapse from a reaction*

<b>Criteria</b>	<b>Relapse</b>	<b>Reaction</b>
Time since completion of treatment	More than 3 years	Less than 3 years
Progression of symptoms and signs	Slow	Fast
Site of skin lesions	In new places	Over old patches
Pain, tenderness, or swelling	No	Yes, skin and nerves
Damage	Occurs slowly	Sudden onset
General condition	Not affected	General ill health

### **Investigation of suspected relapse**

The options for investigating a suspected relapse include:

- Skin smears
- Skin biopsy for histopathological examination if possible.
- Drug sensitivity testing using recently standardized molecular (DNA sequencing) techniques

### **Management of relapse cases**

Suspected relapse cases should be referred to the DTLS/RTLP or one of the leprosy referral centers. Skin smear examinations should be performed on all such cases. Relapse cases should be retreated with the same MDT regimen.

## **Prevention of leprosy**

At the moment, the most important preventive measure against leprosy is early diagnosis of cases and prompt treatment.

- Screening of contacts of known patients provides the opportunity for early diagnosis of cases among them. The programmatic implementation of chemoprophylaxis of contacts without leprosy disease can be done using Single Dose Rifampicin (SDR) as preventive treatment for contacts of leprosy patients (adults and children 2 years of age and above), after excluding leprosy and TB disease, and in the absence of other contraindications.
- BCG vaccination: Several studies have demonstrated protection against both PB and MB leprosy by BCG even though the observed protection has varied between study populations from 20% to 80%. In Uganda, BCG is routinely given to new-borns for its protection against severe forms of TB.

## **TREATMENT OF DRUG RESISTANT LEPROSY**

Leprosy patients with rifampicin resistance should 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. In case of rifampicin plus ofloxacin resistance, a quinolone should not be chosen. Therefore, the recommended regimen is clarithromycin, minocycline and clofazimine for 6 months followed by clarithromycin or minocycline plus clofazimine for an additional 18 months.

*Table 70 Recommended regimens for drug-resistant leprosy*

Resistance type	Treatment	
	First 6 months (daily)	Next 18 months (daily)
Rifampicin resistance	Ofloxacin 400 mg* + minocycline 100 mg + clofazimine 50 mg	Ofloxacin 400 mg* OR minocycline 100 mg + clofazimine 50 mg
	Ofloxacin 400 mg* + clarithromycin 500 mg + clofazimine 50 mg	Ofloxacin 400 mg* + clofazimine 50 mg
Rifampicin and ofloxacin resistance	Clarithromycin 500 mg + minocycline 100 mg + clofazimine 50 mg	Clarithromycin 500 mg OR minocycline 100 mg + clofazimine 50 mg

Because fluoroquinolones are active against TB, leprosy patients starting a second-line regimen should be investigated for signs and symptoms of TB, to ensure that persons with TB are treated with an appropriate regimen effective against both diseases, to avoid emergence of drug-resistant TB. Pharmacovigilance of recommended regimens for resistant leprosy is needed to determine adverse events. This includes electrocardiographic monitoring, due to the risk of QT interval prolongation and associated cardiac arrhythmia, which is associated with exposure to clarithromycin as well as minocycline and quinolones.

Patients treated for resistant leprosy should be registered and their treatment outcomes closely monitored and reported to national authorities and to WHO, to better inform future recommendations on optimal treatment strategies and outcomes for drug-resistant leprosy.

## CONTACT MANAGEMENT OF LEPROSY CASES

The tracing of contacts of newly identified leprosy patients and their screening for signs and symptoms of the disease is a control strategy aimed at reducing transmission to exposed contacts of new cases. People in close and prolonged contact with someone who has leprosy are at high risk of getting infected and potentially infecting others. Early diagnosis is important for two main reasons: to reduce the risk that the patient develops irreversible disability, and to shorten the time the patient can contribute to the transmission of the infection.

### Contacts and definitions

- **Contact Screening** is a synonym of examining a person for signs and symptoms of leprosy with the purpose of detecting leprosy. Screening of contacts may be done at the health facility, at their homes or a designated place. Efforts should be made to maximize the number of contacts traced and screened. Repeat visits may be planned to ensure maximum coverage. Family members of persons affected by leprosy help enhancing coverage of contact screening.
- **Exposure:** When a healthy person comes in contact with a leprosy-infected person able to infect others (i.e., before treatment or even before symptoms occur), the healthy person is considered to be exposed.
- **Infection:** When the leprosy bacillus enters the human body and multiplies, the person is said to be infected. The organism may or may not cause disease, depending on the immunity (the resistance in the body) of the host.
- **Index case:** an untreated patient who may have infected or may still infect others.
- **Contact:** A person having close proximity to a leprosy patient not on treatment for a prolonged duration. Such persons are considered "exposed" to leprosy and may or may not have been infected. "Prolonged duration" is typically defined as having been in contact with an untreated patient for 20 hours per week for at least three months in a year, e.g., family members, neighbours, friends, school children in same class; co-workers in same office, etc.

**NOTE: A person whose exposure with a leprosy patient only starts after the patient has been treated for four weeks is not considered a contact.**

- **Household contact:** contact living in the same dwelling with an index case. This includes family members but also domestic staff or aids or co-workers or others sharing the same accommodation. A family member living elsewhere should not be considered as a household contact.
- **Neighbour contact:** a person living in the neighbourhood of an index case, typically defined as an adjacent household or living within 100 meters. Because of geographic proximity, these persons have a higher probability of being exposed and/or infected.
- **Social contact:** other persons having prolonged contact with an index case and who are not classified as household or neighbour contact. These may include friends, persons sharing workplace (e.g., factory workers, office colleagues) or school (students and teachers)
- **Community contacts:** A community may be defined as a neighbourhood, village, island population, school, workplace, etc., depending on the local conditions and the socio-demographic characteristics of the new leprosy case(s) (e.g., school child, factory worker, etc.). In conditions (e.g., a child leprosy case with disability, a child leprosy case in a low burden setting, populations that are hard to reach, high case detection rate in a small geographical setting a full community screening should be considered for any child leprosy cases with disability a survey should be done to find any remaining hidden child case.

## **Special situations for contact management**

### **1. Contact tracing if the index case is a child**

If the index case is a school going child, disclosing his/her diagnosis and labelling him/her as a cause of potential spread to others may lead to stigma and discrimination. Though a child may spend typically more than 20 hours per week in school, it is not advisable to trace classmates or teachers in the school. The only exception would be if a regular school health programme or a campaign with physical examination is scheduled. This could be an opportunity to investigate leprosy in the school, otherwise the school may be informed and either the school health programme may be roped in or the principal or teacher could be requested to provide the home addresses of the contacts of a child case. Classmates and debridement for ulcers. Specialised protective footwear for anaesthetic feet could also be availed. This footwear helps people with leprosy maintain the ability to walk. This is an innovative solution to the current handmade MCR [microcellular rubber] used by leprosy patients.

### **2. Physiotherapy, occupational therapy,**

Patient education, and counselling for physical rehabilitation and management of disability is key in management of disability due to leprosy. Patients should be taught to inspect parts of their bodies which have lost sensation and see if there are any spots on their hands or feet. They are taught to look for swelling, imminent wounds and report to the hospital if they see the danger signs. Physiotherapy, occupational therapy and podiatric services are provided to all leprosy patients who have disabilities. Moreover, health education on self-care (since patients do not have sensation, lifelong vigilance is required to prevent injury), special splints, and aids and appliances, are provided to all patients who need them.

### **3. Other medical problems**

Longstanding untreated leprosy and chronic ENL reactions lead to medical complications. These patients should be referred to appropriate specialists.

### **4. Psychosocial problems**

Disabilities, as well as beliefs and prejudices concerning leprosy and its causes, are the main sources of psychosocial problems in leprosy patients. People with leprosy often develop low self-esteem and depression as a result of the negative attitudes of their family and community. Such negative attitudes are also observed among some religious leaders and health service providers, including doctors. People suffering from psychosocial problems may need to be referred for counselling or other help.

## **5. Mental Health**

Mental health issues contribute significantly to the wellbeing of people affected by Leprosy. It is essential that mental wellbeing support is provided together with physical care.

The health care worker should support the patient from before, during and after the process of confirming the Leprosy diagnosis.

- Interventions include:
- Group counselling to members of self-care groups can be used to increase mental well-being
- Peer counselling and education regarding human rights should be given to those at risk
- It is important for health care providers to rule out depression and other mental health problems to improve detection of people who need mental health care.
- NOTE: if depression is diagnosed, treatment should be given appropriately
- Provision of mental health services should put in consideration the gender and cultural background of persons affected by leprosy

## **PREVENTION OF DISABILITY (POD) AND SELF-CARE**

- Early diagnosis and prompt treatment of leprosy prevents occurrence of disabilities.
- The extent of disability at the time of diagnosis should be assessed for every patient.
- Recent nerve damage can be reversed with corticosteroid treatment.
- Grading of leprosy-related disability on a scale from 0-2 guides programmatic decisions on prevention and management of disabilities.
- Prevention and management of disabilities among individual patients includes aspects to be managed at home, in the nearest health facility, or at higher levels of the referral system.

### **Patients at greater risk of nerve damage**

Patients experiencing long delays between the appearance of the first symptoms of leprosy and the start of treatment are at greater risk of nerve damage. Early diagnosis and treatment of leprosy prevents the occurrence of long-term complications. MB patients with impaired nerve function at diagnosis should be monitored more closely. Nerve damage can occur during MDT and after the patient has completed MDT. The risk declines steadily over the following three years. The effects of nerve damage in leprosy.

Recent nerve damage (present for less than six months) can usually be reversed with the use of steroids. Many patients present with nerve damage of very long duration, from which no further recovery is expected.

The common physical problems resulting from nerve damage that affect people with leprosy are described in Table 71.

Table 71 Common physical problems and aims of appropriate POD action

<b>Problem</b>	<b>Signs</b>	<b>Secondary effects</b>	<b>Aims of POD action</b>
Weakness and incomplete closure of eyes	Dryness, ulceration of cornea, and scarring	Impairment of vision, blindness	Preservation of sight
Loss of sensation in the hand	Dryness, cracking, and ulceration	Loss of tissue, joint stiffness	Keeping the skin in good condition and avoiding injury
Weakness and deformity of the hand	Visible deformity	Contracture and fixed deformities	Preservation of muscle strength and prevention of contractures and deformities
Loss of sensation and ulceration of the foot	Dryness, cracking, and ulceration	Chronic infection	Keeping the skin in good condition Provision of protective footwear Prevention of injury
Weakness and deformity of the foot	Foot drop	Ulceration and permanent deformity	Preservation of muscle strength and prevention of deformity

### Care for people with disabilities due to leprosy

Interventions for disabilities are carried out at the following levels:

- Home-based care, including those activities that can be done by the person at home.
- Local health facility.
- Referral services (requiring the input of specialists).

### Home-based care for patients

Patients should be taught how to carry out these self-care activities:

#### i. Problems with eye closure

- Inspect the eye in a mirror to check for redness (if no mirror, ask a neighbour to check)
- Learn to blink frequently to keep the eyes moist and exercise the lids
- Wear a hat with a large brim and/or sunglasses to prevent dust from getting into the eyes
- Use a sheet or mosquito net to cover the head at night

#### ii. Problems with hands and/or feet

- Inspect daily for signs of injury
- Soak the hand/foot in water for about 30 minutes every day
- Use a rough stone to smoothen the dead skin
- Apply oil or petroleum jelly when the skin is still wet to prevent the skin from drying out
- Use a clean cloth to cover any open wound
- Walk as little as possible, and walk slowly. Take frequent rests (foot care)
- If foot ulcers are present, rest is essential
- If there is any muscle weakness, such as foot drop, passive stretching and active exercises help to prevent contracture and may assist muscle strengthening
- Use protective footwear (e.g., microcellular rubber sandals) all the time for insensitive feet and protective appliances (e.g., gloves) for insensitive hands

## **Lower-Level health facility interventions**

The next level of interventions can be carried out in a Health Centre III or IV. The health workers should

- Discuss the management of their patients' disability problems with the district supervisor, but eventually take over the responsibility for implementing the interventions
- Instruct and assist the patient in carrying out the relevant home-care activities above.

### **i. Problems with eye closure**

- Provide artificial tears or any eye ointment (not containing steroids) if the eyes are very dry
- Treat conjunctivitis with antibiotics
- Refer more serious eye problems to an Ophthalmology Clinical Officer, Ophthalmologist or the nearest specialist eye clinic

### **ii. Problems with the hand**

- Review to assess the implementation of expected home-care activities and advise as necessary
- Refer, if required

### **iii. Problem with the foot**

- Review to assess the implementation of expected home-care activities and advise as necessary
- Take foot maps for protective footwear or arrange for these to be taken by the DTLS or trained community-based rehabilitation worker
- Refer, if required

## **Interventions conducted at a regional referral centre**

### **i. Problems with the eyes**

- Management of acute eye problems at eye clinic
- Corrective surgery in severe cases of lagophthalmos (with cornea exposed)
- Cataract surgery (leprosy is not a contraindication to cataract surgery).

### **ii. Problems with the hand**

- Instruction and assistance with adaptation of tools to avoid injury to insensitive hands.
- Removal of thick callus and trim ulcers with a scalpel blade.
- Splinting of joints in the presence of weakness or contractures.
- Management of severe infection of hand ulcers.
- Reconstructive surgery to correct some cases of weakness or claw-hand (as long as the joints remain mobile).

### **iii. Problems of the foot**

- Removal of thick calluses and trimming of ulcers with a scalpel blade.
- Management of severe infections of foot ulcers.
- Surgical management of chronic ulcers.
- Provision of orthopaedic appliances, including those for foot drop.
- Surgical correction of foot drop.

## **Encouraging people to practice self-care at home**

It is important that individual patients be given self-care instructions that are relevant to their particular situation and that they are supported to practice self-care at home. Such support may be provided by:

- Health workers
- Family members
- Local community-based organizations
- Community development extension workers
- Self-care groups for people affected by leprosy or living with disabilities from other causes

## **The value of appropriate footwear for people affected by leprosy**

The use of appropriate footwear is important for preventing ulceration among people with loss of feeling in their feet. The shoes should be locally available, socially acceptable and used whenever patients walk. The NTLP-recommended footwear for people with loss of sensation in their feet is microcellular rubber (MCR) sandals, with a firm under-sole, a soft insole, and heel straps. Velcro straps are preferred to other kinds of fastenings. Other shoes meeting the basic criteria can be used.

## **REHABILITATION**

Rehabilitation is the process of helping an individual achieve the highest level of function, independence, and quality of life possible.

Rehabilitation includes all measures aimed at reducing the impact of disability on an individual, enabling him or her to achieve independence, social integration, a better quality of life, and self-actualization." UN Standard Rules for Equalization of Opportunities for Persons with Disabilities (PWD).

- People affected by leprosy, especially those with disability, have physical, functional and social economic rehabilitation needs
- Health service providers are responsible for identifying such needs and assuring access to the appropriate rehabilitation services
- The rehabilitation needs of people affected by leprosy should be addressed in by services available for all other people using the CBR approach

## **The role of health workers in rehabilitation**

Whereas health workers and some district supervisors may not have the time or expertise to be involved in rehabilitation activities, they are expected to:

- Identify physical, functional, or socioeconomic problems resulting from disability among patients under their care
- Know about available services for rehabilitation including those providing assistive devices
- Know how to refer people to make use of those services
- Advocate for people affected by leprosy to access health care and rehabilitation in the same way as others
- Discourage restrictive thoughts and ideas of other health workers

Table 72 : Examples of services to which people with disability can be referred

<b>Problem</b>	<b>Rehabilitation services required</b>
Deformity of the hand	Exercises, reconstructive surgery, peer support
Foot drop	Ankle-foot appliance, reconstructive surgery
Amputee	Artificial limb, wheelchair
Depression	Counselling
Mobility limitation	Crutches, walking stick, wheelchair, white cane
Stigma in the family	Counselling
Exclusion from community activities	Education, advocacy, and promotion of inclusion
Poverty	Microcredit for self-employment or income generation

### **Community-Based Rehabilitation**

Community-based rehabilitation (CBR) is defined as a strategy within general community development for the rehabilitation, equalization of opportunities, and social inclusion of all people with disabilities.

Leprosy may lead to variety of physical, functional, and social and/or economic problems needing different types of physical and social economic rehabilitation. To address these, comprehensive approaches that maximize benefits for the individual, family and society at large are needed.

CBR is one such approach. It emphasizes community participation and empowerment of the individuals involved. CBR requires the full participation of the clients, their families, and the communities in the rehabilitation process. While people with disabilities may need temporary referral to specialized services (e.g., for provision of assistive devices or appliances), these should be linked to CBR programs.

Organizations of people with disabilities need to be involved in the planning and management of rehabilitation services.

Persons affected by leprosy who are in need of rehabilitation should have access to existing general rehabilitation services. Similarly, any existing leprosy-specific rehabilitation services should be extended to people with other disabilities.

### **Principles of Community Based Rehabilitation**

- Inclusion – work to remove all barriers that block persons affected by leprosy from access to the mainstream of society.
- Participation – focuses on ability, not disabilities and depends on the participation and support of family members and local communities.
- Empowerment – persons affected by leprosy take leadership roles within programmes.
- Equity –emphasize equal opportunities and rights; equal citizenship.
- Raising Awareness – address attitudes and behaviour within the community, developing understanding and support for people affected by leprosy and ensuring sustainable benefits.
- Self-Advocacy – consistently involves people affected by leprosy in all issues related to their well-being.
- Facilitation – uses multisectoral collaboration to support the community and addresses the individual needs of persons affected by leprosy. With ultimate aim of an inclusive society.
- Gender sensitivity ansd special needs – depends on effective partnerships with community-based organizations
- Partnership – activities must be sustainable beyond immediate life of the programme itself.

## Promoting inclusion of persons affected by leprosy in CBR

The following actions may assist in formulating a CBR strategy at district level:

- Develop a district plan for community-based rehabilitation that conforms to the national policy/plan
- Prepare guidelines for mobilizing local resources to provide special services from government and non-governmental organizations
- Establish a network of services
- Develop the capacity of service providers and mechanisms to create awareness about leprosy- related disabilities among people with disabilities
- Promote a team approach for service provision
- Introduce locally-specific techniques to train and develop skills and knowledge of people with disabilities and their families
- Promote opportunities for educational, functional, and vocational training and job-placements
- Involve people with disabilities and their families in the decision-making process

## MONITORING OF LEPROSY CONTROL

- A focused monitoring and evaluation system is required for the continuous assessment of the leprosy control status in the district, region, and country
- Leprosy control services are monitored based on two main sets of indicators
- In order to gather monitoring information for the leprosy control program, it is essential to use additional tools than those of the mainstream HMIS
- The quality of monitoring information is determined by the accuracy, completeness, and timeliness of data collection especially in the treatment facility.

## Leprosy Control Indicators

Leprosy control indicators include the following categories:

- Those for monitoring progress in leprosy control
- Those for assessing quality of leprosy services

## Indicators for measuring progress in leprosy control

- Indicators for measuring progress include general (core) indicators and those intended for evaluating case-finding activities in particular.
- The number of new cases in the district is used to estimate the amount of MDT required for that district during the following year. Depending on the methods used for case detection, the annual figures over a period of several years will show if there is an increase or decrease, which in turn indicates whether leprosy control activities are effective. Calculating the case detection rate makes it possible to compare one area with another.
- The number of cases with Grade 2 disabilities detected in a population gives an indication of under-detection.
- The proportion of new cases with Grade 2 disabilities among all new cases detected during the year is used to assess the delay in diagnosis as an indicator for quality of case detection activities.
- The proportion of new cases with Grade 2 disabilities per 100,000 populations at national level is used to indicate the contribution by leprosy to disability in the general population.
- If transmission of leprosy is being reduced in an area, it is expected that the number of child leprosy cases (below the age of 15) will decrease. This trend should be monitored over several years. It is also used for estimating the required stock of child MDT blister packs. The proportion of new child cases with Grade 2 disabilities is a further indicator of the quality of case detection activities.
- Some districts diagnose leprosy more frequently in men than women, but there is concern that women may have less access to health care in some districts. If a male-to-female ratio of higher than 2 is observed, steps should be taken to ensure that women have adequate access to diagnostic services.
- The number and proportion of MB cases among new cases is a useful guide to the cases at risk of complications and is used for estimating the required quantities of MDT drugs.

*Table 73 Indicators for measuring progress in leprosy control*

Progress in Leprosy control								
No.	Indicator	Calculation	Data Source	Level			Frequency	
				District	Region	National	Quarterly	Annual
1	Number of new leprosy cases	Count absolute number	Leprosy registers	×		×		×
2	Case detection rate	Number of new leprosy cases/ Total population*100,000	District quarterly reports on leprosy control			×		×
3	Number of new cases with Grade 2 disability	Count absolute number of new cases with Grade 2 disability	District quarterly reports on leprosy control	×		×	×	×
4	Proportion of new cases with Grade 2 disability	Number of new cases with Grade 2 disability/ Total number of new cases *100	District quarterly reports on case finding	×		×		×
5	Proportion of new cases with Grade 2 disability per 100,000 population	Number of new cases with Grade 2 disability/ Total population * 100,000	District quarterly reports on case finding			×		×
6	Proportion of new PB cases who complete MDT	Number of new PB cases who complete MDT	District quarterly reports on treatment outcomes	×		×		×

\*See box 6 on how to calculate MDT completion rates

## **Indicators for assessing the quality of leprosy services**

The indicators for quality of leprosy services, summarized in Table 74 below, will be collected at regional level:

- The proportion of new cases that are correctly diagnosed is an indication of the capacity of the health system to detect new cases. The Regional TB/Leprosy Focal Person will validate the diagnosis of at least 50 percent of the new cases reported in the region or make arrangements with a suitable other person to do so. In regions with less than 10 new cases, all new cases should be validated. Validation should be performed within three months of starting the patient on MDT.
- This exercise will help to identify areas where additional training and/or supervision is required.
- The proportion of new patients who complete their treatment on time is an indication of how well the leprosy patients are being served by the health services. The rate is calculated separately for PB and MB patients in a cohort analysis. A cohort is a group of patients who all started treatment in the same batch (in the same quarter). The total of the figures from the four quarters in a year will give the annual report.
- The NTLP Central Unit will be responsible for organizing confirmation of reported suspected relapse cases and their management.
- The proportion of patients who develop new or additional disability during MDT is an indicator to measure how well new nerve damage is detected and treated. Information for calculating this indicator will be collected using the EHF (eye-hand-foot) score. In order
- The NTLP Central Unit will be responsible for organizing confirmation of reported suspected relapse cases and their management
- The proportion of patients who develop new or additional disability during MDT is an indicator of how well new nerve damage is detected and treated. Information for calculating this indicator will be collected using the Eye-Hand-Foot (EHF) score which should be calculated and recorded at diagnosis and then repeated at the time when treatment is completed.

### *Box 4 How to calculate leprosy treatment (MDT) completion rate*

- For PB completion rate, the cohort will be from the same quarter 1 (one) year ago.
- Identify all the PB patients who are new cases in the district register and who started MDT in the reporting quarter 1 (one) year back. Note this number.
- From the cohort, count the number who completed treatment within 9 (nine) months of registration
- The PB treatment completion rate is calculated as follows:

$\frac{\text{Number of new PB cases who completed MDT}}{\text{Number of new PB cases who started MDT}} \times 100$

$\frac{\text{Number of new PB cases who completed MDT}}{\text{Number of new PB cases who started MDT}} \times 100$

- For MB completion rate, the cohort will be from the same quarter 2 (two) years ago:
- Identify all the MB patients who were new cases in the register and who started MDT in the reporting quarter 2 (two) years back. Note this number
- From this cohort, count the number who completed treatment within 18 months of registration.
- The MB treatment completion rate is calculated as follows:

$\frac{\text{Number of new MB cases who completed MDT}}{\text{Number of new MB cases who started MDT}} \times 100$

$\frac{\text{Number of new MB cases who completed MDT}}{\text{Number of new MB cases who started MDT}} \times 100$

Table 74 Indicators for quality of leprosy services

No.	Indicator	Calculation	Source of data	Level			Frequency	
				District	Region	National	Quarterly	Annual
1	Proportion of new cases correctly diagnosed	(Number of new cases validated as correctly diagnosed (within 3 months of registration))/ (Total number of new cases validated) x 100	Activity reports		x	x	x	x
2	Proportion of new PB cases who complete MDT *	(Number of new PB cases who complete MDT)/ (Total number of new PB cases who started MDT 1 year ago) x 100	District quarterly reports on treatment outcomes			x	x	x
3	Proportion of new MB cases who complete MDT*	(Number of new MB cases who complete MDT)/ (Total number of MB cases who started MDT 2 years ago) x 100	District quarterly reports on treatment outcomes	x		x	x	x
4	Number of relapses	Record absolute number of relapses after MDT	Leprosy registers District quarterly reports	x		x	x	x
5	Proportion of patients who develop new or additional impairments/disabilities during MDT	(Number of cases with increased EHF score)/(Total number of cases started on MDT 1or 2 years earlier) x100	District leprosy register			x	x	x
6	Proportion of new MB cases who complete MDT*	Number of new MB cases who complete MDT/Total number of MB cases who started MDT 2 years ago *100	District quarterly reports on treatment outcomes	x		x		x
7	Proportion of new child cases	Total number of new child cases/ Total number of new cases x 100	Leprosy registers District quarterly reports	x		x		x
8	Number of new child cases with Grade 2 disability	Absolute number of new child cases with Grade 2 disabilities at diagnosis	District quarterly reports on case finding	x		x		x
9	Proportion of new female cases	Total number of new female/ Total number of new cases *100	Registers and quarterly reports			x		x
10	Proportion MB cases	Total number of new MB cases/ Total number of new cases (PB+ MB) *100	Registers and quarterly reports on case-finding			x		x
11	Proportion of Leprosy patients who have TB	<b>Numerator:</b> Total number of leprosy patients with TB <b>Denominator:</b> Total number of new leprosy patients	Registers and Quarterly reports			x		x
12	Proportion of New leprosy patients who are HIV positive	<b>Numerator:</b> Total Number of new leprosy patients with are HIV positive. <b>Denominator:</b> Total number of new leprosy patients	Registers and quarterly reports on case-finding			x		x
13	Proportion of index leprosy cases for which contact tracing and screening have been done	<b>Numerator:</b> Total Number of new index leprosy patients contact traced <b>Denominator:</b> Total number of new index patients	Registers and quarterly reports on case-finding			x		x
14	Proportion of screened and eligible contacts who receive Leprosy Post exposure Prophylaxis (LPEP)	<b>Numerator:</b> All eligible contacts screened and given LPEP <b>Denominator:</b> All Leprosy contacts Screened	Registers and quarterly reports on case-finding			x		x

## Annex



### HMIS FORM 100: NOTIFICATION OF DEATH AND CERTIFICATION OF CAUSE OF DEATH

#### Instructions

1. This form is filled by a medical practitioner
2. The purpose of this form is to notify death and certify the exact cause of death
3. Complete the form in duplicate, enter the data in DHIS2 and submit a copy to MRA after verification and declaration.

(a) Details of Deceased Surname, Given Name, Other names (full name) .....

NIN  Deceased Category  N  R  F Deceased Nationality.....

Occurrence of the event of death "if death occurred in community, or at time of arrival to facility" (skip to section of Manner of death)

(b) Residential Address of Deceased at time of death

Village..... Parish..... Sub-County..... County..... District..... Occupation.....

Date of Birth..... Age..... Sex..... Place of Death..... Date of Death..... Time of Death..... p.m./a.m.

#### Frame A: Medical data: Part I and 2

Report disease or condition directly leading to death on line a  Report chain of events 'due to' (b to d) in order (if applicable)  State the underlying cause on the lowest used line	   	Cause of death	Time interval from onset of condition to death
		a Due to:	
		b Due to:	
		c Due to:	
d Due to:			
2. Other significant conditions contributing to death (time intervals can be included in brackets after the condition)			

#### Frame B: Other medical data

Was surgery performed within the last 4 weeks	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown
If yes, please specify date of surgery			
If yes, please specify reason for surgery (disease or condition)			
Was an autopsy requested?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown
If yes were the findings used in the certification	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown

#### Frame C: Manner of death:

<input type="checkbox"/> Disease	<input type="checkbox"/> Assault	<input type="checkbox"/> Could not be determined					
<input type="checkbox"/> Accident	<input type="checkbox"/> Legal intervention	<input type="checkbox"/> Pending investigation					
<input type="checkbox"/> Intentional self-harm	<input type="checkbox"/> War	<input type="checkbox"/> Unknown					
If external cause or poisoning:	Date of injury	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8 <input type="checkbox"/> 9 <input type="checkbox"/> 10					
Please describe how external cause occurred (If poisoning please specify poisoning agent)							
Place of occurrence of the external cause:							
<input type="checkbox"/> At home	<input type="checkbox"/> Residential institution	<input type="checkbox"/> School, other institution, public administrative area	<input type="checkbox"/> Sports and athletics area				
<input type="checkbox"/> Street and highway	<input type="checkbox"/> Trade and service area	<input type="checkbox"/> Industrial and construction area	<input type="checkbox"/> Farm				
<input type="checkbox"/> Other place (please specify):	<input type="checkbox"/> Unknown						
Fetal or infant death							
Multiple pregnancy	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown				
Stillborn	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown				
If death within 24h specify number of foetus survived	<input type="checkbox"/>	Birth weight (in grams)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>				
Number of completed weeks of pregnancy	<input type="checkbox"/>	Age of mother (years)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>				
If death was perinatal, please state conditions of mother that affected the fetus and newborn							
For women, was the deceased pregnant?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown				
<input type="checkbox"/> Pregnant at time of death	<input type="checkbox"/> Died within 42 days after delivery.						
<input type="checkbox"/> Between 43 days up to 1 year before death	<input type="checkbox"/> Unknown						
Did the pregnancy contribute to the death	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown				
Referred from (level of care)	<input type="checkbox"/> Health Facility	Parity	<input type="checkbox"/> Don't Know	Mode of delivery	<input type="checkbox"/> SVD	<input type="checkbox"/> Assisted	<input type="checkbox"/> Caesarean
Place of Delivery	<input type="checkbox"/> Health Facility	<input type="checkbox"/> Home	<input type="checkbox"/> In transit	Delivered by skilled attendant	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Don't Know

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