TB Guidelines 2021 Summarised

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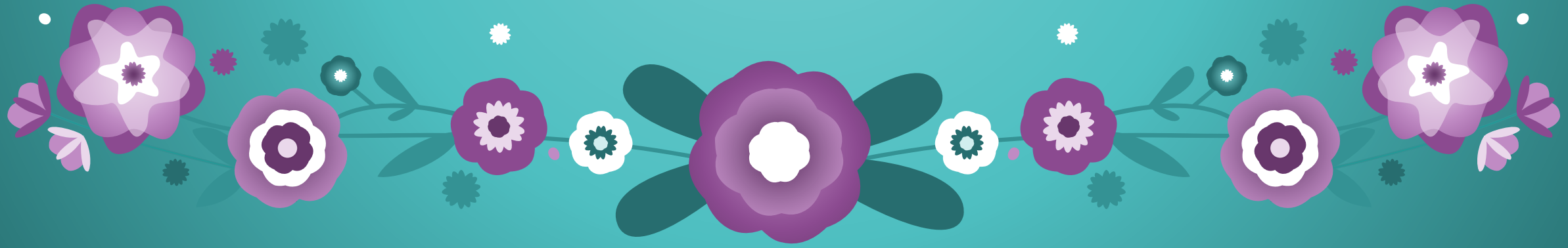


All patients should undergo the following;

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

3.2 Classification of Tuberculosis

3.2.1 TB Case Definitions

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

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

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

c) **A clinically diagnosed TB case;** A clinically diagnosed TB case is one who does not fulfill the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation. **Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.** All such cases should be notified regardless of whether TB treatment was started or not.

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

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

This classification is summarized in the table below:

Table 3.1: Classification of TB

1. Classification based on anatomical sites	
Pulmonary TB (PTB)	Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. This exclude pleural effusion
Extra pulmonary TB (EPTB)	Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lung parenchyma, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.
2. Classification based on history of previous TB treatment (patient registration group)	
New patients	Patient who has never been treated for TB or has taken anti-TB drugs for less than 1 month.

Previously treated patients	Patient who has received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment as follows: a) **Relapse patients**; previously treated for TB, declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection). b) **Treatment after failure patients**; previously treated for TB and whose treatment failed at the end of their most recent course of treatment. c) **Treatment after loss to follow-up patients**; previously treated for TB, and declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as return after default patients).
Patients with unknown previous TB treatment history	Manage as a previously treated patient
3. Classification based on HIV status	
HIV-positive TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has a positive result from HIV testing conducted at the time of TB diagnosis or other documented evidence of enrolment in HIV care, such as enrolment in the pre-ART register or in the ART register once ART has been started.
HIV-negative TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has a negative result from HIV testing conducted at the time of TB diagnosis. Any HIV-negative TB patient subsequently found to be HIV-positive should be reclassified accordingly.
HIV status unknown TB patient	Any bacteriologically confirmed or clinically diagnosed case of TB who has no result of HIV testing and no other documented evidence of enrolment in HIV care. If the patient's HIV status is subsequently determined, he or she should be reclassified accordingly.
4. Classification based on drug resistance (refer to DR TB chapter)	
Drug Susceptible TB	Any bacteriologically confirmed case of TB with no evidence of resistance to any of the first line anti-TB medicines
Drug Resistant TB	Any bacteriologically confirmed case of TB with confirmed resistance to any of the first line medicines. It also includes cases with confirmed resistance to second line anti-TB medicine.

3.3 Diagnosis of Tuberculosis

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

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

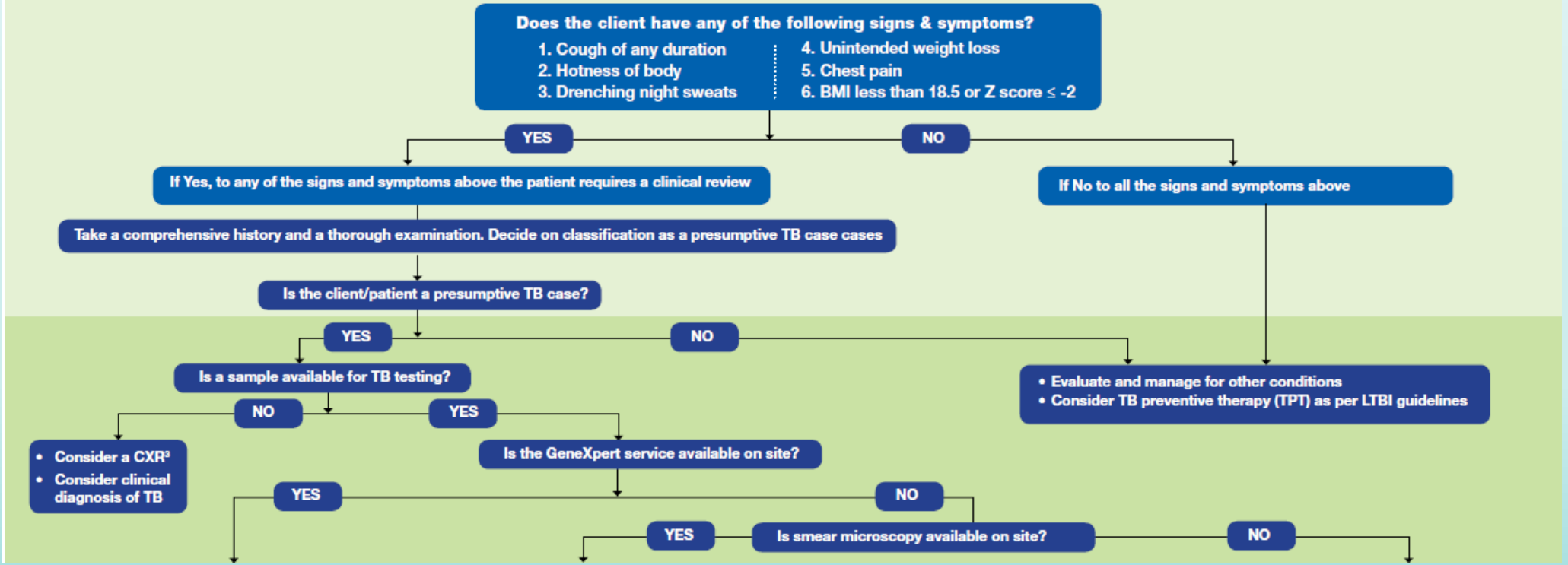
Persons who screen positive for any of the signs and symptoms listed above should undergo a thorough clinical evaluation before classification as a presumptive TB case. Presumptive TB cases should undergo diagnostic evaluation as per the TB screening and diagnostic algorithm for adults and adolescents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

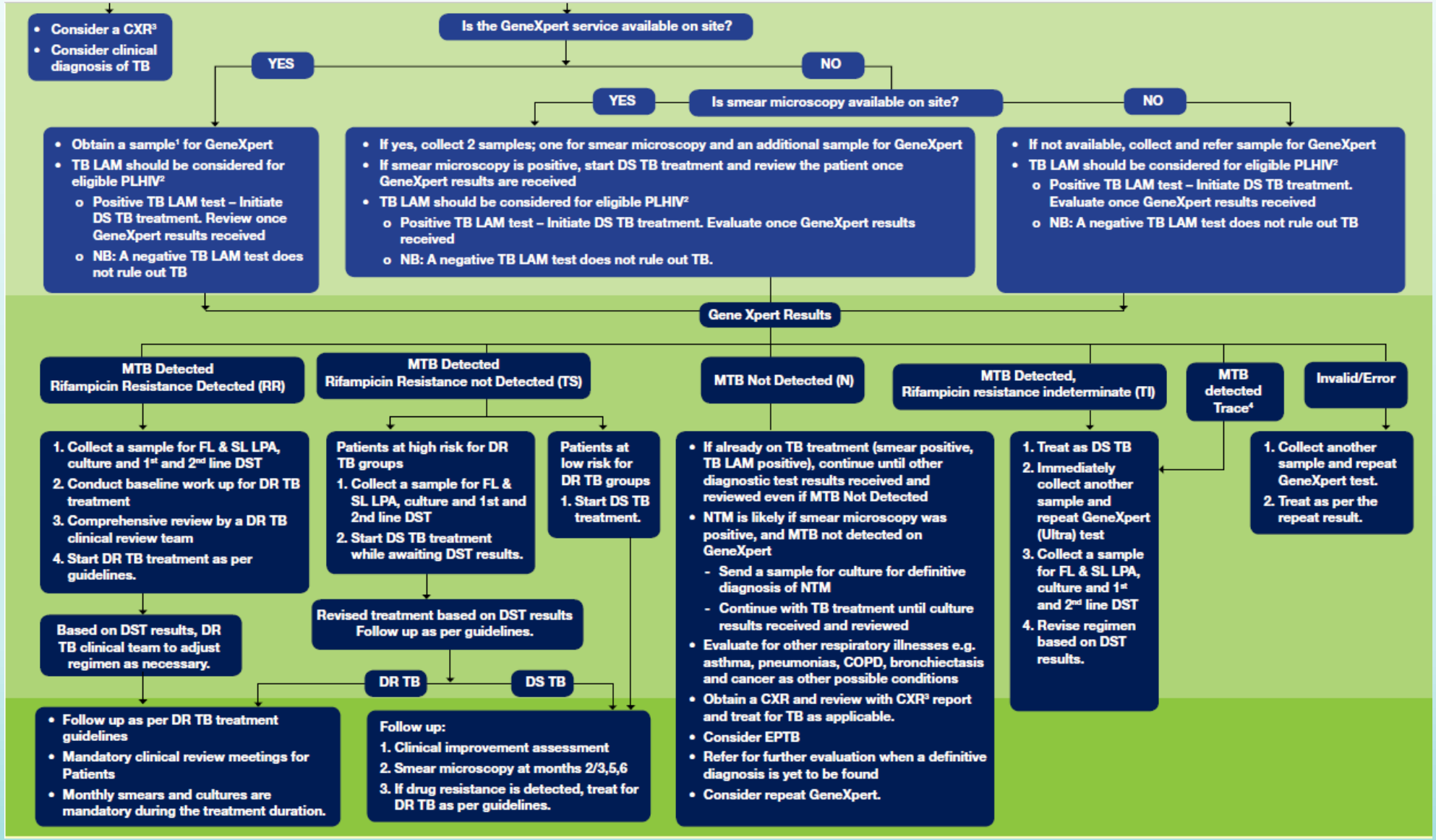
REPUBLIC OF KENYA

MINISTRY OF HEALTH

TB SCREENING AND DIAGNOSTIC ALGORITHM FOR CHILDREN ≥10yrs AND ADULTS

GeneXpert is the recommended initial test for TB diagnosis. However, where a facility has no GeneXpert, smear microscopy SHOULD BE USED as another sample is collected & referred for GeneXpert.
TB LAM should be used where indicated among PLHIV as per guidelines. TB LAM SHOULD NOT be used as an alternative to GeneXpert testing.




Consider a CXR[3]
Consider clinical diagnosis of TB
Is the GeneXpert service available on site?
YES
NO
YES
Is smear microscopy available on site?
NO
Obtain a sample[1] for GeneXpert
TB LAM should be considered for eligible PLHIV[2]
Positive TB LAM test – Initiate DS TB treatment. Review once GeneXpert results received
NB: A negative TB LAM test does not rule out TB
If yes, collect 2 samples; one for smear microscopy and an additional sample for GeneXpert
If smear microscopy is positive, start DS TB treatment and review the patient once GeneXpert results are received
TB LAM should be considered for eligible PLHIV[2]
Positive TB LAM test – Initiate DS TB treatment. Evaluate once GeneXpert results received
NB: A negative TB LAM test does not rule out TB.
If not available, collect and refer sample for GeneXpert
TB LAM should be considered for eligible PLHIV[2]
Positive TB LAM test – Initiate DS TB treatment. Evaluate once GeneXpert results received
NB: A negative TB LAM test does not rule out TB
Gene Xpert Results
MTB Detected Rifampicin Resistance Detected (RR)
MTB Detected Rifampicin Resistance not Detected (TS)
MTB Not Detected (N)
MTB Detected, Rifampicin resistance indeterminate (TI)
MTB detected Trace[4]
Invalid/Error
1. Collect a sample for FL & SL LPA, culture and 1st and 2nd line DST
2. Conduct baseline work up for DR TB treatment
3. Comprehensive review by a DR TB clinical review team
4. Start DR TB treatment as per guidelines.
Patients at high risk for DR TB groups
1. Collect a sample for FL & SL LPA, culture and 1st and 2nd line DST
2. Start DS TB treatment while awaiting DST results.
Patients at low risk for DR TB groups
1. Start DS TB treatment.
If already on TB treatment (smear positive, TB LAM positive), continue until other diagnostic test results received and reviewed even if MTB Not Detected
NTM is likely if smear microscopy was positive, and MTB not detected on GeneXpert
- Send a sample for culture for definitive diagnosis of NTM
- Continue with TB treatment until culture results received and reviewed
Evaluate for other respiratory illnesses e.g. asthma, pneumonias, COPD, bronchiectasis and cancer as other possible conditions
Obtain a CXR and review with CXR[3] report and treat for TB as applicable.
Consider EPTB
Refer for further evaluation when a definitive diagnosis is yet to be found
Consider repeat GeneXpert.
1. Treat as DS TB
2. Immediately collect another sample and repeat GeneXpert (Ultra) test
3. Collect a sample for FL & SL LPA, culture and 1st and 2nd line DST
4. Revise regimen based on DST results.
1. Collect another sample and repeat GeneXpert test.
2. Treat as per the repeat result.
Based on DST results, DR TB clinical team to adjust regimen as necessary.
Revised treatment based on DST results Follow up as per guidelines.
DR TB
DS TB
Follow up as per DR TB treatment guidelines
Mandatory clinical review meetings for Patients
Monthly smears and cultures are mandatory during the treatment duration.
Follow up:
1. Clinical improvement assessment
2. Smear microscopy at months 2/3,5,6
3. If drug resistance is detected, treat for DR TB as per guidelines.

Footnotes

[1] Samples for GeneXpert - sputum, CSF, Pleural aspirate, Peritoneal fluid, synovial fluid, Gastric Aspirate, Nasopharyngeal aspirate, FNA, Lymph node biopsy, Pus, stool

[2] Indications for use of TB-LAM, as an adjunct test to GeneXpert:

- PLHIV with advanced disease (WHO stage 3 or 4 or CD4 count ≤200 cells/ mm^3 (or ≤25% for children ≤5years old) with presumed TB
- PLHIV that have any danger signs of severe illness: respiratory rate >30 breaths per minute, temperature >39°C, heart rate >120 beats per minute, unable to walk unaided
- Currently admitted to hospital

[3] All CHEST X-rays should be reported and the reports reviewed by the clinician for definitive management. Refer to the CXR algorithm for TB diagnosis

[4] MTB detected Trace – Results from sample with few bacilli (paucibacillary TB). Rifampicin resistance status.

HIV Testing, using the HTS algorithm 1, is recommended during TB screening and diagnosis.

Screening for diabetes is recommended among all adult patients with TB disease

Key			
CXR	Chest X-ray	**LPA**	Line Probe Assay
DR TB	Drug Resistant TB	**MTB**	Mycobacteria Tuberculosis
DS TB	Drug Susceptible TB	**NTM**	Non-Tuberculous Mycobacteria
DST	Drug Susceptibility Testing	**TST**	Tuberculin skin test
EPTB	Extra pulmonary TB	**SL**	Second line
FL	First line		

DR TB risk classification among patients
High risk for DR TB*
1. All previously treated TB patients: treatment failures, relapses, treatment after loss to follow up
2. Contacts of Drug Resistant TB patients
3. TB patients with a positive smear result at month 2 or month 5 of TB treatment
4. Patient who develops TB symptoms while on IPT or has had previous IPT exposure
5. Healthcare Workers with TB symptoms
6. Prisoners with TB symptoms
7. Refugees with TB symptoms
Low risk for DR TB
All presumptive TB cases who are **NOT** in the high risk group

*ALL the high risk patients **MUST** be prioritized to receive DST - Genexpert, FL and SL LPA, culture and FL and SL DST.

Not important ☺

DS TB follow up and DR TB surveillance	
POSITIVE SMEAR RESULT AT	**Action**
Month 2/3	• Evaluate for **adherence**, and other causes of **delayed conversion** • Request for **all** the following **drug susceptibility tests** (DST); GeneXpert, FL LPA and SL LPA. Culture and FL and SL DST • **Continue with RHZE** for one more month, or longer if DST results not received by then • Adjust treatment regimen based on DST results • Repeat smear microscopy at end of month 3. If smear positive continue with RHZE and review DST results and inform the SCTLC immediately • Do not proceed to the continuation phase (RH) without a DST result confirming susceptibility to RH (rifampicin and isoniazid)
Month 5 or month 6	• **Declare treatment failure** and stop anti-TB treatment • Review by the sub county and county TB clinical review teams • Evaluate for adherence, other causes of delayed conversion and treatment failure • Request for GeneXpert, FL LPA and SL LPA. Culture and FL and SL DST • Review DST results and re-initiate treatment based on DST results and other clinical findings
DR TB follow up and DR TB surveillance	

Smear positive or culture positive at month 3 or later	• Evaluate for **adherence**, and other causes of **delayed conversion**
	• Request for the following **drug susceptibility tests** (DST) (GeneXpert, Culture and First Line (FL) and SL DST, FL LPA and SL LPA) depending on the initial resistance pattern
	  ○ Review by the sub county and county clinical review teams
	  ▪ Evaluate for adherence, other causes of reversion and treatment failure
	  ▪ Review the DST results
	  ○ Declare failure if at the end of the extended intensive phase (refer to DR TB guidelines)
	  ○ Send a case summary to the national clinical team after review by the county clinical team
	• Do not proceed to the continuation phase (depending on treatment regimen) without a DST result

Smear positive smears and/or cultures during continuation phase	• Declare treatment failure
	  ○ Review by the sub county and county clinical review teams
	  ▪ Evaluate for adherence, other causes of reversion and treatment failure
	  ▪ Review the DST results
	• Send a case summary to the national clinical team after review by the county clinical team

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

A) History Taking

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

Table 3.2: Differential Diagnosis of Pulmonary Tuberculosis

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

B) Physical Examination

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

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

C) Investigations for Diagnosis of PTB

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

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

Flowchart ishhhh

Table 3.3: Tuberculosis Investigations

Investigation	Target	Purpose
1.GeneXpert and GeneXpert ultra	Preferred test of choice for all presumptive TB cases	For diagnosis of TB and detection RR TB
2.Smear microscopy (Fluorescent and Light microscopy)	All presumptive Pulmonary TB where GeneXpert is not available All DSTB patients for treatment follow up.	Detect TB disease. Monitoring of bacteriologically confirmed TB patients on treatment at months 2/3, 5 and 6
3. Chest X-ray	Preferred for all presumptive pulmonary and some extra pulmonary TB where accessible and affordable	A screening tool to identify those at high risk of TB disease. Supports TB diagnosis especially in children and when sputum for AFB/ GeneXpert is negative or not applicable
4. Histology	All presumptive EPTB	Tissue diagnosis in suspected EPTB e.g. TB adenitis
Other supportive tests		
Tuberculin skin test and IGRA	For detection of TB infection	Used in detection of latent TB infection
Lateral flow urine lipoarabinomannan assay (LF-LAM)	HIV infected patients with severe illness or advanced disease All hospitalized PLHA	For diagnosis of TB as an add-on test to GeneXpert/ GeneXpert ultra It is an add-on test to GeneXpert testing to increase diagnostic yield of TB testing in severely immunocompromised PLHA.
All attempts must be made to make a bacteriological diagnosis of PTB in adults.		

3.4 Baseline Work Up for Newly Diagnosed Tuberculosis

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

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

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

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

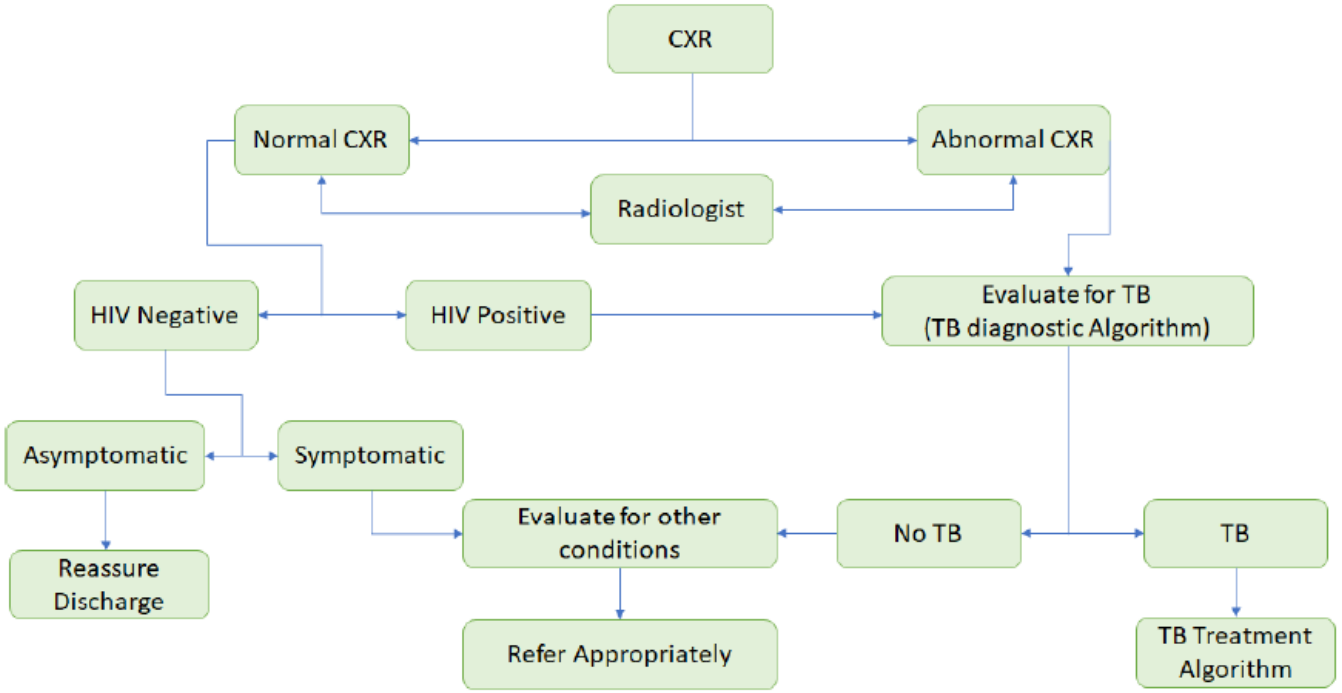
Mouthing.....

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

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

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

Figure 3.2: Chest X-ray Algorithm for TB diagnosis



3.5.1 Recommended Radiographic Views and Utility

Standard Views	
View	**Indication**
Postero-anterior (PA)	Standard View for All adults
Antero-posterior (AP)	For patients unable to stand including the very sick, elderly and children
Additional Views (to be recommended by the radiologist)	
Lateral	As an aid to PA and AP view to evaluate the mediastinum, hilar regions, the posterior lung and spine
Lordotic	To evaluate subtle changes in the lung to provide better visualization.
Apical	To evaluate subtle changes in the Apical segments of the upper lobes to provide better visualization
Lateral decubitus	To rule out small pleural fluid in the presence of blunting of the costophrenic angles

Osce ishh.....

3.5.3 Radiographic Findings in Pulmonary Tuberculosis

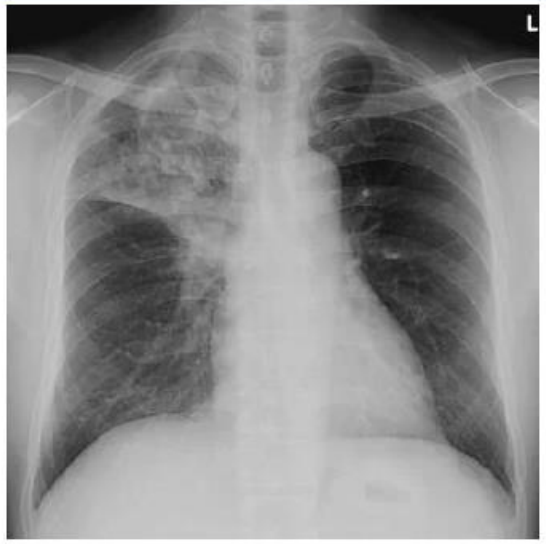
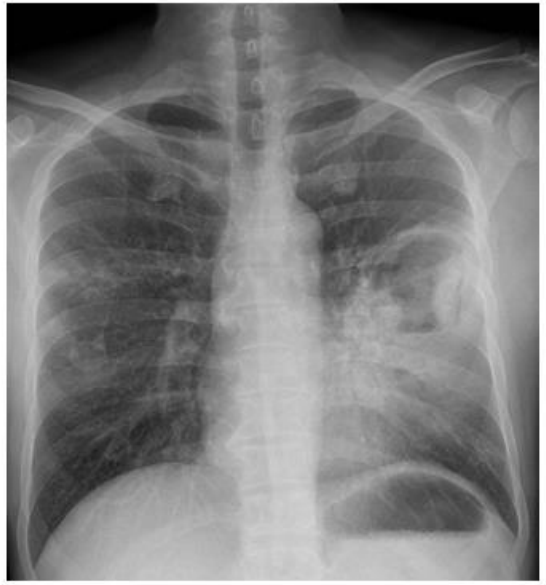
Tuberculosis disease exhibits a varied range of radiographic patterns in the lung depending on the patient immunological status, exposure whether recent or past and duration of infection. It can be primary or post primary, typical or atypical.

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

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

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

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

Radiograph	
	**Findings** Right apical consolidation, cavitation and fibrotic changes with elevation of the minor fissure.
	Left lingula segment consolidation and cavitation. Intracavitary aspergillosis is also a possibility. Right mid zone parenchymal infiltrates and nodules are also demonstrated

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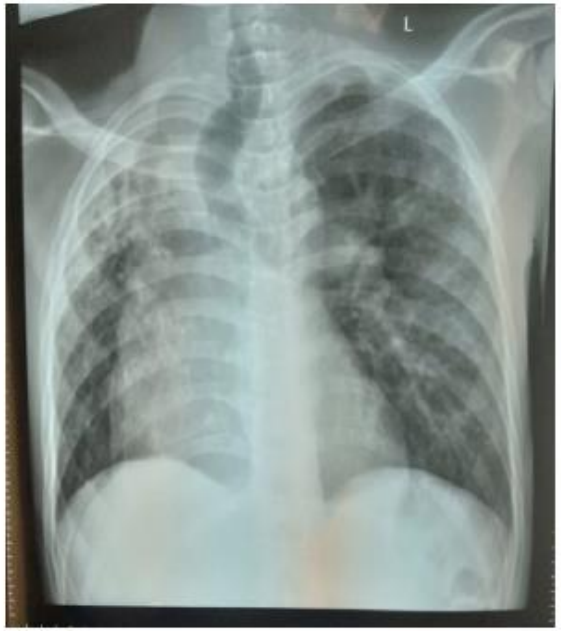	Right sided fibrosis with marked volume loss/ retraction of the upper lobe. Right apical thick irregular pleural capping. Left upper lobe nodular lesions and a cavitary lesion.

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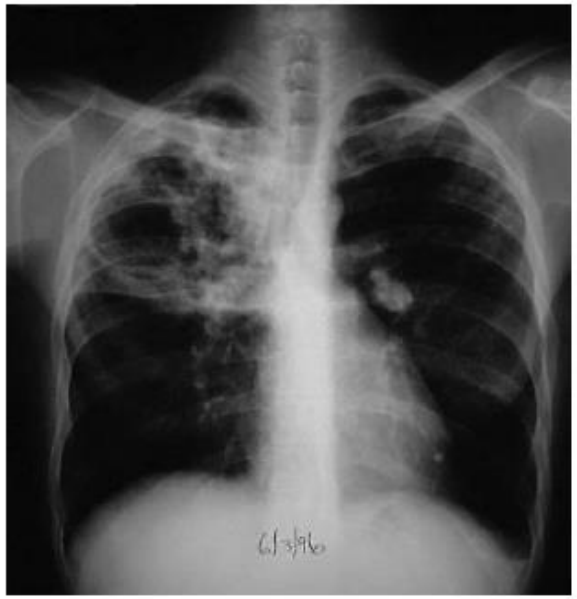
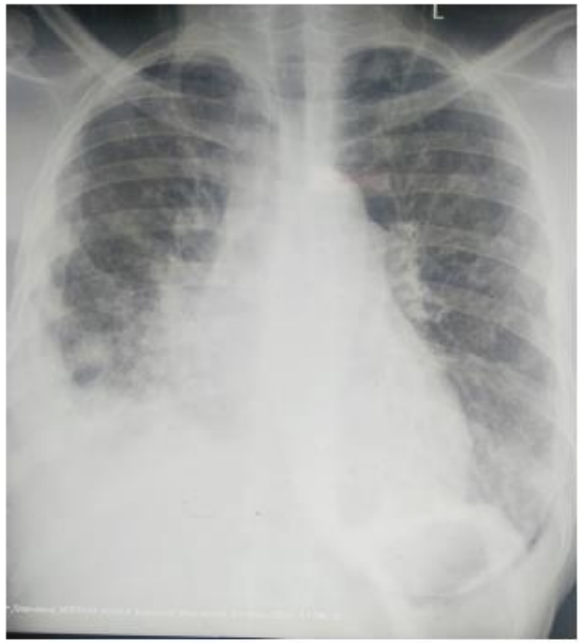
	Right upper lobe consolidation, cavitary lesions and fibrosis.
	Diffuse parenchymal infiltrates and nodular lesions. Right pleural effusion. Cardiomegaly

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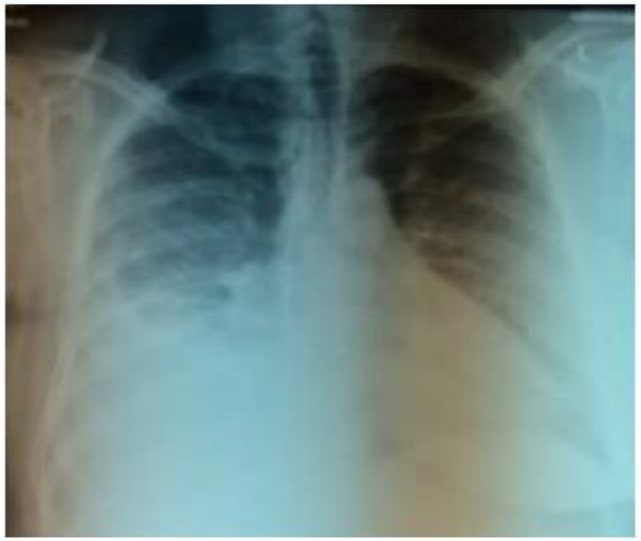
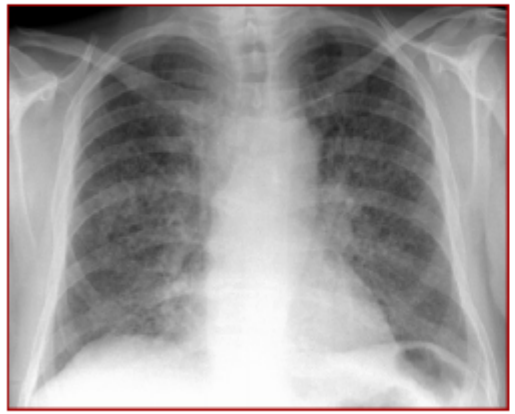
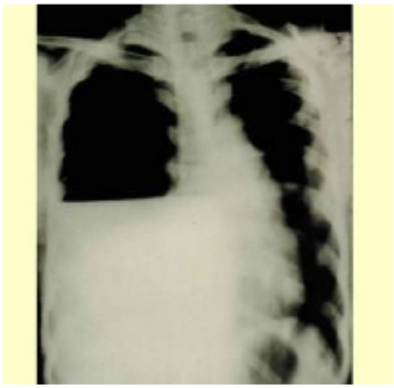
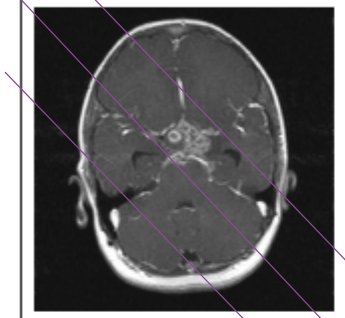
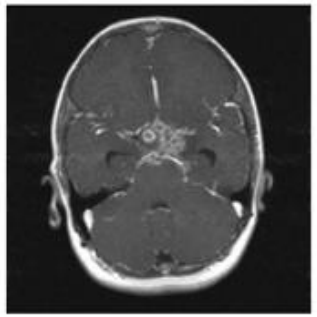
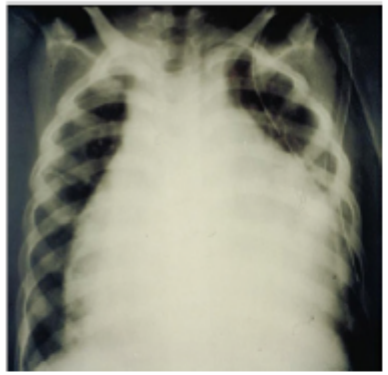
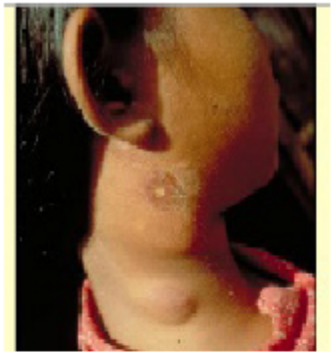
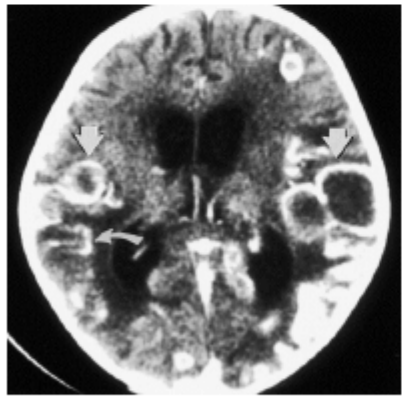
	Right pleural effusion. Parenchymal infiltrates. Cardiac patient.
Miliary TB 	• Miliary TB with Miliary lesions on chest X-ray.

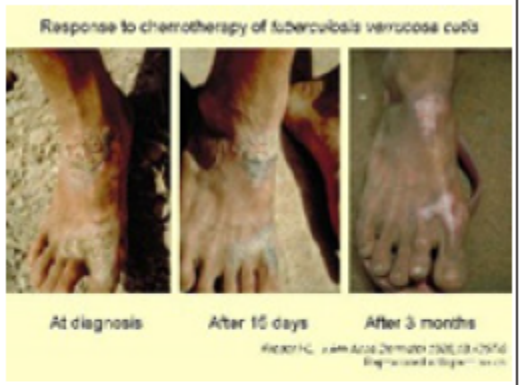
Table 3.6: Common Forms of Extrapulmonary TB and Diagnostic Approach

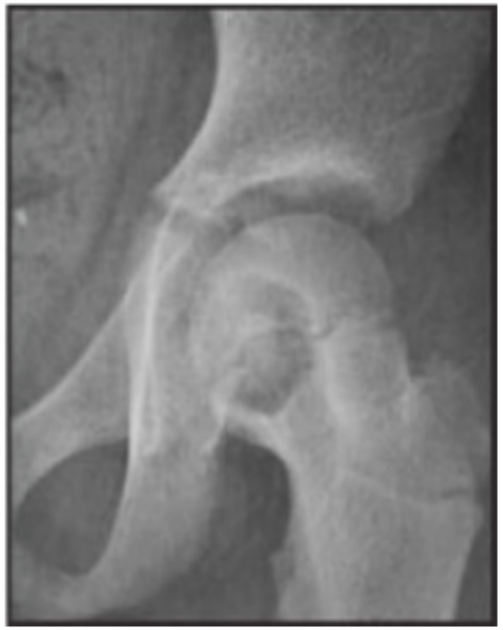
Form of Extra Pulmonary TB	Signs and Symptoms	Diagnosis
Pleural TB with Pleural Effusion 	Tuberculous pleural effusion usually presents with: • Local chest symptoms that include chest pain, Shortness of breath. • Cough and systemic symptoms including fever and night sweats. • "stony" dullness on percussion • Reduced breath sounds on the side of the effusion.	• Chest x-ray is often required to confirm the presence of the effusion. When effusion is small a supplemental lateral decubitus view or ultrasound on the suspected side of effusion may be performed. • It is also advisable, if the expertise exists, to always perform a diagnostic pleural aspiration at the minimum to distinguish pus (empyema) from "usual" effusion. Aspirated fluid should be sent to the laboratory for cytology and microbiological tests including GeneXpert and TB Culture. • A pleural biopsy is rarely required in young patients below the age of 40 years. • Older patients and especially those with a significant smoking history may have other diagnoses and in these patients it is advisable to perform a pleural biopsy using an Abrahm's needle.

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

Tuberculous Pericarditis 	Tuberculous pericarditis is increasingly becoming common in the HIV era and it may present with a variety of symptoms including: • Shortness of breath (the most common symptom). • Chest pain. • Cough. • Leg swelling. • Fever. • Usually has a high pulse rate (tachycardia). • May have a low blood pressure, impalpable apex beat, quiet heart sounds and signs of heart failure like a large liver, ascites and leg edema.	• A chest x-ray is always required and usually shows **a large globular heart**. • Where feasible patients suspected to have a pericardial effusion should be referred to a heart specialist for confirmation of the diagnosis using echocardiography. • A pericardial tap for diagnostic purpose is rarely required but may be life saving if there are signs of cardiac compression (tamponade). This procedure must be done by experienced health care workers (cardiologists) only.

TB adenitis 	• Tuberculous adenitis is one of the common types of extra-pulmonary TB • Usually unilateral • Most common site is the cervical area • Painless swelling –initially discrete then matted • Fistula and sinus formation	• Node aspirate • Node biopsy for both histology and culture
TB encephalitis including Tuberculoma 	The clinical presentation is similar to that of other space occupying brain lesions and includes: • Headaches. • Vomiting. • Convulsions. • Limb weakness. • Cranial nerve palsies.	• Brain CT scans are useful in demonstrating lesions such as tuberculomas or cerebral infarcts. • MRI with contrast and spectroscopy is superior in the diagnosis of encephalitis, tuberculoma and spinal TB . • Often it is difficult to confirm the diagnosis of brain TB and most patients are treated on an empiric basis.

TB of the skin		
	• *Lupus vulgaris:* Persistent and progressive form of cutaneous TB. It occurs as small sharply defined reddish-brown lesions with a gelatinous consistency (called apple jelly nodules). • Untreated, lesions persist for years, leading to disfigurement • *Scrofuloderma:* Skin lesions result from direct extension of underlying TB infection of lymph nodes, bone or joints. • Often associated with TB of the lungs. Firm, painless lesions that eventually ulcerate with a granular base. May heal even without treatment but this takes years and leaves unsightly scars.	• The diagnosis is usually made or confirmed by a skin biopsy. Typical tubercles are caseating epithelioid granulomas that contain acid-fast bacilli. These are detected by tissue staining, culture and polymerase chain reaction (PCR)

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

3.7 Treatment of Drug Susceptible Tuberculosis

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

3.7.1 Goals of TB Treatment

The overall goals of TB therapy include:

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

3.7.2 Principles of TB treatment

The principles of TB treatment include the following:

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

3.7.3 First line Anti-Tuberculosis Drugs

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

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

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

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

- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol

These drugs are given in two phases of treatment:

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

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

Table 3.7: Grading of Activity of Anti-Tuberculosis Drugs

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

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

Advantages of using FDCs include:

1) Reduced risk of resistance developing to the drugs in the event of missed doses.
2) Reduction of pill burden.
3) Fewer medication errors.
4) Fewer prescription errors.
5) Easier for treatment supporter to monitor treatment via DOT

Disadvantages of using FDCs include:

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

3.7.5 Adult TB First Line Treatment Regimens

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

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

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

Table 3.11: Dosages for Pyridoxine

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

a) Hospitalization:

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

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

b) Steroid Therapy:

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

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

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

Table 3.13: Treatment Outcomes for Drug Susceptible TB Patients

Outcome	Definition
Cured	A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
Treatment success	The sum of cured and treatment completed. This is calculated based on bacteriologically confirmed cases.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Moved to Cat. 4 (MT4)	A patient who is confirmed to have Drug resistant TB while on first line TB treatment regimen.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.

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

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

Months of treatment	Specimen	Test	Result	Comment/action
				• Request for **all** the following **drug susceptibility tests** (DST); GeneXpert, FL* LPA and SL** LPA, Culture, FL DST and SL DST. • If DST results is received by then adjust treatment regimen based on DST results accordingly

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

** FL - First Line*

***SL - Second Line*

Steps to take for treatment interruption include:

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

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

NOTE:

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

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

Table 3.17: Management of Treatment Interruption in Tuberculosis Treatment

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

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

a) Adverse Effect: Acute Hepatotoxicity

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

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

Suggested management strategy

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

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

b) Adverse Effect: Peripheral Neuropathy

Causative agent: **Isoniazid**

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

Symptomatic relief for peripheral neuropathy:

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

c) Adverse Effect: Optic Neuritis

Causative agent: **Ethambutol**

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

Suggested management strategy

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

Table 8.1: Pathways of Drug-Resistant TB development

1.Natural Resistance	2.Primary Resistance	3.Acquired Drug Resistance
- Occurs when all live species reach a certain number of divisions -They undergo random genomic mutations giving rise to organisms with certain altered functions	-A patient is infected with a resistant strain of the bacilli.	-Due to inadequate therapies leading to selection of mutant resistant strains-it's an expression of poor treatment

Table 8.2. Factors associated with Drug-Resistant TB Development

Healthcare factors	Drugs related factors	Patient-related factors
• Non-compliance to guidelines • Inadequate training • Poor treatment monitoring • Poorly organized or funded TB control programs	• Inadequate supplies • Poor quality • Poor storage conditions • Wrong dose or combinations • Poor regulation of medicines • Unavailability of certain medicines	• Poor adherence or poor DOT • Lack of information • Lack of transportation • Adverse effects • Social barriers • Malabsorption

Table 8.3: Classification based on the Resistance pattern:

Resistance pattern	Definition
Presumptive drug-resistant TB case	These are Individuals with a higher risk of getting drug resistant TB than the general population. They include: smear-positive previously treated patients such as relapse, return after default (RAD) and failure; new smear-positive pulmonary TB patients whose sputum remains smear-positive at month 2; symptomatic close contacts of the known MDR-TB patient, refugees, prisoners, health care workers with symptoms of TB, DR TB contacts.
Monoresistance	Resistance to one first-line anti-TB medicine only.
Poly-drug resistance (PDR)	Resistance to more than one first-line anti-TB medicine (other than both Isoniazid and Rifampicin)
Multi-drug resistance (MDR)	Resistance to at least both Isoniazid and Rifampicin
Rifampicin resistance(RR)	Resistance to Rifampicin detected using phenotypic or genotypic methods, with or without other anti-TB drugs. It includes any resistance to Rifampicin, whether mono resistance, multidrug resistance, Poly-drug resistance or extensive drug resistance.
Isoniazid resistance	Refers to Mycobacterium tuberculosis strains with resistance to isoniazid and susceptibility to rifampicin confirmed in vitro
Pre-XDR	Resistance to Isoniazid and Rifampicin and either a fluoroquinolone or a second-line injectable agent but not both.
Extensive drug resistance (XDR)	Resistance to any Fluoroquinolone and at least one of three second-line injectable drugs (Capreomycin, Kanamycin and Amikacin), in addition to multidrug resistance.

Table 8.5: Classification based on the Anatomical site

Classification	Definition
Pulmonary Drug resistant TB	Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. This exclude pleural effusion -Milliary TB is classified as PTB because the lesions are in the lungs. -Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra pulmonary TB. **-A patient with both pulmonary and extra pulmonary TB should be classified as a case of PTB**
Extra pulmonary Drug Resistant TB	Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lung parenchyma, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

People at high risk for DR TB include:

1. DR TB contacts with symptoms of TB. Includes children with TB symptoms who are contacts of DR TB source persons.
2. Failures on Drug susceptible TB treatment (smear positive at month 2 and 5)
3. Patients who develop TB while on IPT
4. Health care workers with TB symptoms.
5. Refugees with TB symptoms
6. Prisoners with TB symptoms
7. All previously treated patients. They include, failures, relapses, return after loss to follow ups.

8.5.3 Classification of anti TB drugs used in the management of DR-TB

The 2019 WHO classification of anti-TB drugs used in the management of DR-TB is based on their efficacy and experience for use as described in the table below.

Table 8.9: Grouping Medicines for use in the treatment of drug-resistant TB

Group	Medicine	Abbreviation
Group A Include all three medicines (Unless the cannot be used)	Levofloxacin or Moxifloxacin	Lfx Mfx
	Bedaquiline	Bdq
	Linezolid	Lzd
Group B Add both medicines (Unless they cannot be used)	Clofazimine	Cfz
	Cycloserine or Terizidone	Cs Trd

Group C Add to complete the regimen and when medicines from Group A and B cannot be used	Ethambutol	E
	Delamanid	Dlm
	Pyrazinamide	Z
	Imipenem/Cilastatin or Meropenem	Imp/Cln Mpn
	Amikacin or (Streptomycin)	Am (s)
	Ethionamide or Prothionamide	Eto Pto
	p-amino salicylic acid	PAS

NOTE

- This new classification is intended to guide the design of longer individualized regimens; however, majority of DRTB patients will be on standardized regimens.
- Medicines in Group A and C are shown in decreasing order of usual preference for use (most preferred comes first)
- Always use Carbapenems e.g. Imipenem/Cilastatin together with Clavulanate
- Group C drugs should only be added to complete the regimen and when medicines from Group A and B cannot be used.

8.5.4 Treatment regimens by resistant patterns

The Injectable free treatment regimen:

It is the recommended regimen for MDR/RR and Pre-XDR (resistant to SLIs) TB patients including adults, children and pregnant women. The Drugs used in these regimens are administered orally.

This regimen has two phases:

1. **Intensive phase**: 6 months

The end of intensive phase is defined by a negative culture at the end of the 3rd month and three consecutive negative smears taken 30 days apart after month 3. This phase may be extended in **consultation** with the National PMDT to 7 and/or 8 months in any of the following situations

a) Slow clinical response to treatment after clinical evaluation, characterized by:
    i. Ongoing /worsening TB (pulmonary) symptoms (cough, fever, drenching night sweats and weight loss/poor weight gain)
    ii. Worsening radiological features i.e. cavities, infiltrates, opacities

b) Delayed smear or culture conversion

c) Cases where baseline SL LPA results are indeterminate/FLQ susceptibility is not confirmed.

A negative culture at month 4 and negative smears at the end of month 7and/or 8 month marks the END of the extended intensive phase and **should not** be extended further.

2. **Continuation phase**: 12 months

The continuation phase starts from month 7 as determined by culture/smear results or at the end of the extended intensive phase where applicable. The continuation phase is 12 – 14 months depending on the DST pattern. Reversion of sputum cultures (from negative to positive) indicates treatment failure. In case of reversion, a multi-disciplinary team should urgently review the patient and the national clinical team informed as soon as possible.

Table 8.10: Kenya DR-TB treatment regimens according to resistant patterns

Pattern of Drug Resistance	Regimen	Duration
MDR/ RR TB	Intensive phase: 6 Bdq/Cfz/Lfx/Cs/Lzd Continuation phase: 12 Cfz/Lfx/Cs	18 months
Pediatric MDR / RR TB (<6yrs and <25kg)	Intensive phase: 6 Mfx/Cfz/Cs/Lzd Continuation phase: 12 Mfx/Cfz/Cs	18 months
Pre-XDR - Injectable resistant	Intensive phase: 6 Bdq/Cfz/Lfx/Cs/Lzd Continuation phase: 12 Cfz/Lfx/Cs/	18 months
Pre-XDR - Fluoroquinolones Resistant	**Intensive phase: 6Bdq/Dlm/Lzd/Cfz/Cs/** **Continuation phase: 14 Dlm/Cfz/Cs**	20 months
ISONIAZID mono resistance	**6 RZE/Lfx** **(with pyridoxine)**	6 months
Bedaquiline Intolerance (In cases of Severe Adverse Events or hypersensitivity)	**Intensive Phase: 6 Dlm/Lzd/Lfx/Cfz/Cs** **Continuation phase: 12 Lfx/Cfz/Cs**	18 months
Poly-drug resistance (PDR TB) (HE/HEZ +-S)	**9 RZE/Lfx** **(with pyridoxine)**	9 Months
Pyrazinamide mono-resistance(Z) Or Pyrazinamide and Ethambutol (EZ) without INH resistance Or Ethambutol Mono-resistance(E)	**2 RHZE** **4 RH** **(with pyridoxine)**	6 months
Extensively Drug-resistance (XDR)	**Individualized regimen**	18-24 months
Any case excluded from any of the regimens above	**Individualized regimen**	18-24 months

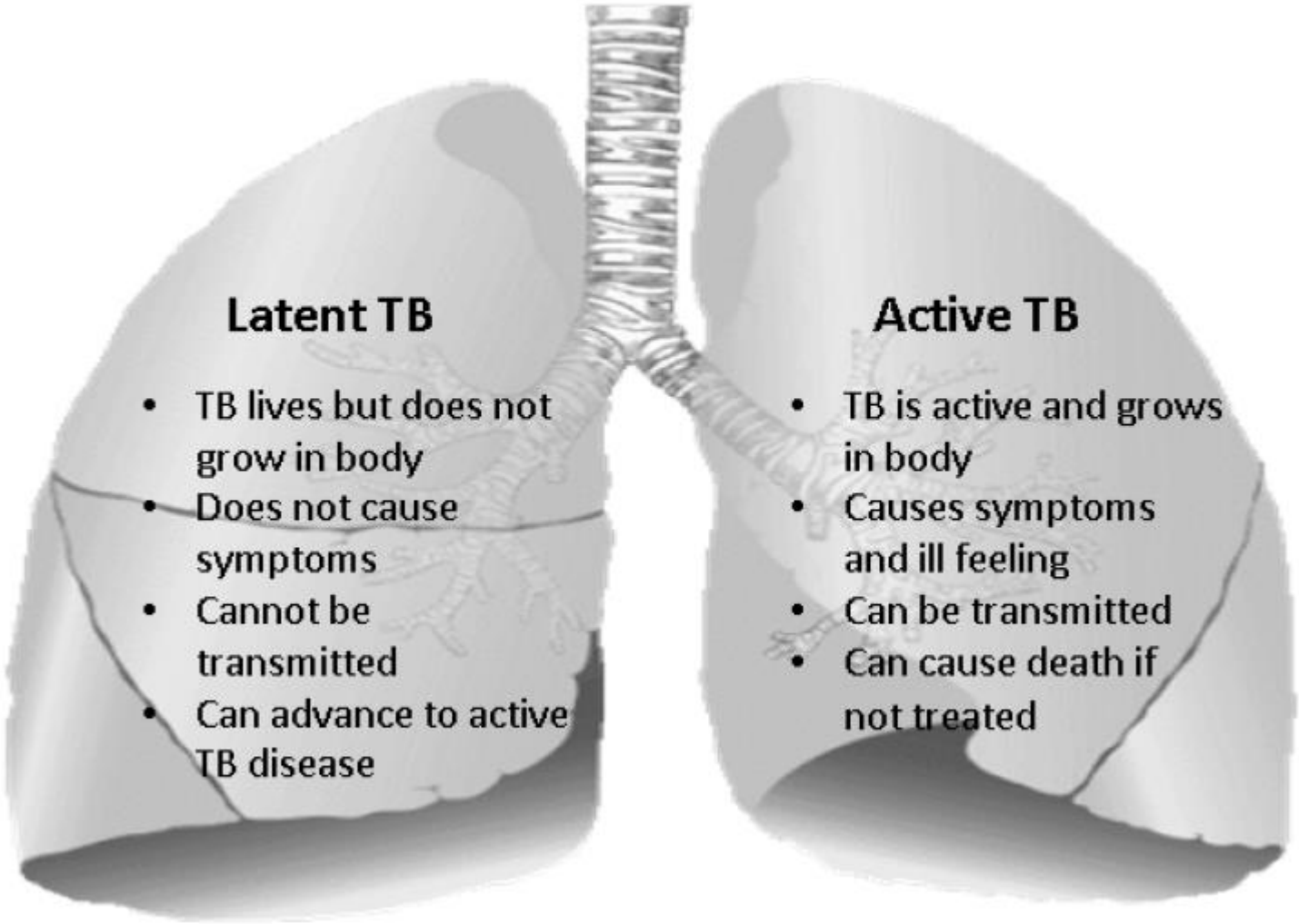
Introduction

Latent TB infection (LTBI) is a state of persistent immune response to stimulation by *M. tuberculosis* antigens with no evidence of clinically manifestation of active TB. It is estimated that approximately one-quarter of the world's population (about 1.3 billion people) have LTBI and 5-10% of these are at risk of progression to active TB disease over the course of their lives, most of them within the first 5 years after initial infection.

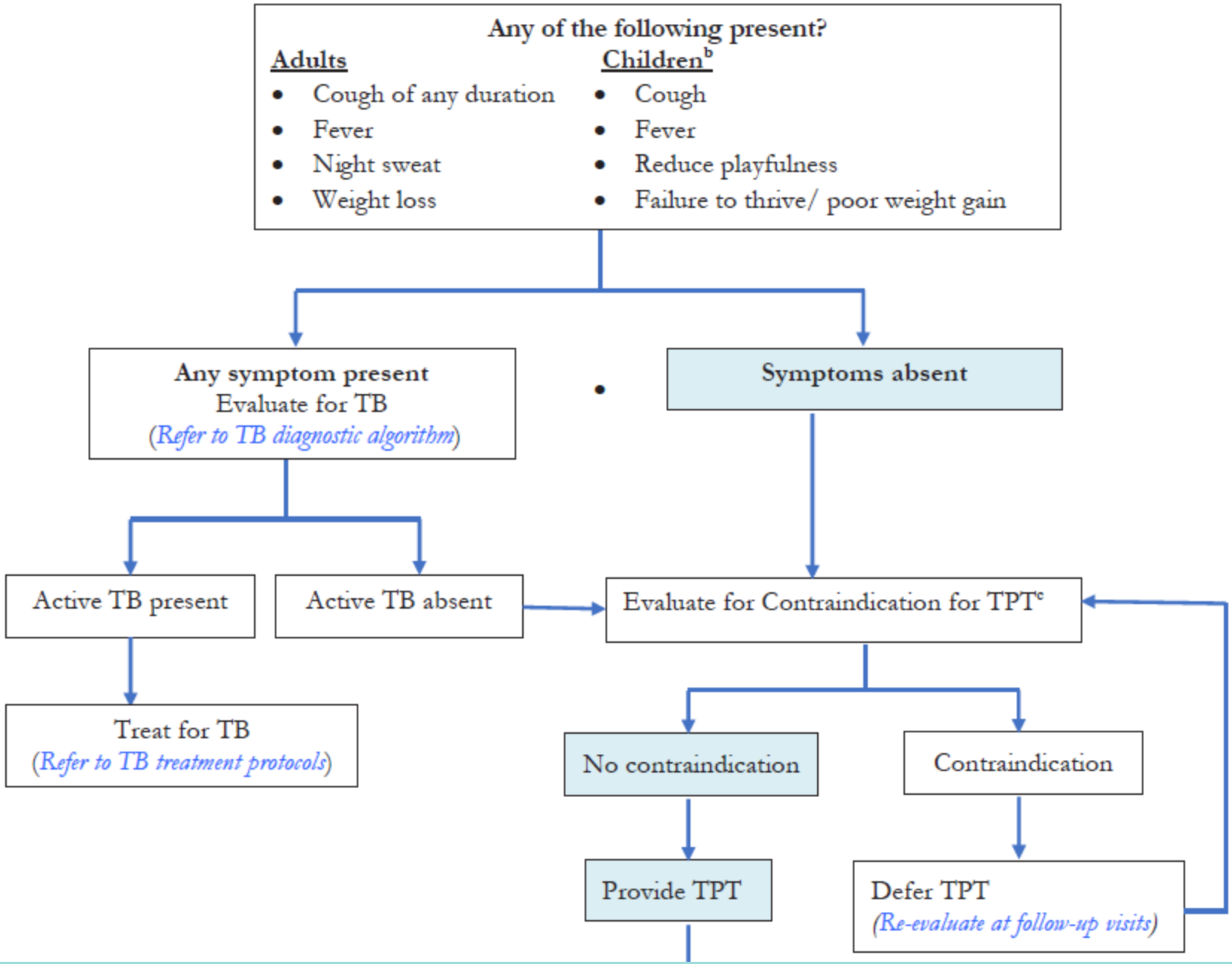
When a person inhales the air that contains droplets with M. tuberculosis bacilli, most of the larger droplets become lodged in the upper respiratory tract (the nose and throat). However, smaller droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection may begin. In the alveoli, some of the tubercle bacilli are killed, but a few multiply in the alveoli and enter the bloodstream and spread throughout the body. Bacilli may reach any part of the body. Within 2 to 8 weeks, however, the body's immune system usually intervenes, halting multiplication and preventing further spread. The immune system is the system of cells and tissues in the body that protects the body from foreign substances. At this point, the person has latent TB infection (LTBI).

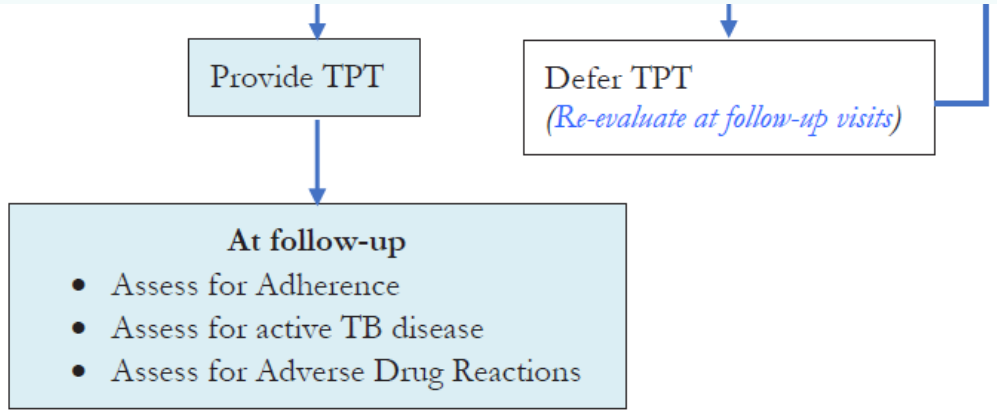
The risk of progression to active TB disease after infection depends on several factors, the most important being immunological status such as HIV, severe malnutrition, patients on immunosuppressive therapy etc. Provision of TB Preventive Therapy (TPT) has proven itself an effective intervention to avert the development of active TB disease, with efficacy ranging from 60% to 90%.

Table 11.1: Difference between Latent TB Infection and Active TB Disease



Algorithm for Tuberculosis Preventive Therapy (TPT) in individuals at risk[a]





TPT Treatment Options			
Age category	**HIV status**	**Treatment Options**	**Frequency[d]**
<15 years	HIV negative	3RH (Rifampicin/Isoniazid)	Daily for 3 months
	HIV positive	6H (Isoniazid)	Daily for 6 months
≥15 years	Regardless of HIV status	3HP (Isoniazid/Rifapentine)	Once weekly for 3 months
If 3HP or 3RH is contraindicated or In Pregnancy		6H	Daily for 6 months
Pyridoxine is given with all of the above options			

Note:

a. Individuals at risk are: PLHIV, household contacts of bacteriologically confirmed pulmonary TB, healthcare workers, prisoners, patients on dialysis, on cancer treatment, undergoing organ or haematological transplant and those with silicosis
b. Child – a person under the age of 10 years
c. Contra-indications for TPT include active hepatitis (*acute or chronic*), symptoms of peripheral neuropathy and chronic alcohol abuse
d. Refer to dosing charts for appropriate dose

LTBI testing by TST or IGRA is not a requirement for initiating TPT in PLHIV and child household contacts aged <5 years. However, it *may* be provided prior to TPT to the rest of the at-risk population if available and does not delay or hinder access to TPT.

Table 11..2: Recommended regimens for TPT and their indications.

TPT Regimen	Indications	Further considerations
Rifapentine and isoniazid (3HP) Once Weekly for three months *(12 doses)*	• Adult PLHIVs excluding patients on PI-based ARV regimens • All household contacts of Bacteriologically confirmed pulmonary TB patients, who are aged ≥15 years • Health care workers Prisoners and staff in prison settings • Other adult population at risk (e.g., patients undergoing chemotherapy, patients on dialysis, patients undergoing transplant, patients with silicosis)	• There is currently insufficient data to support the use of RPT and INH in pregnancy • Rifapentine can decrease levels of hormonal contraception • INH should not be given to persons with known pre-existing liver damage to avoid an additive effect on liver dysfunction • INH can cause peripheral neuropathy. Vitamin B6 helps prevent peripheral neuropathy
Rifampicin plus Isoniazid (3RH) Daily for 3 Months *(84 doses)*	• HIV negative children aged <15 years who are contacts of Bacteriologically confirmed pulmonary TB patients	
Isoniazid (6H) Daily for 6 months *(168 doses)*	• Adult PLHIV on PI-based ARV regimens • All CLHIV aged below 15 years Any patient with intolerance or contraindication to 3HP or 3RH • Pregnant women	

Note: *All TPT regimens should be offered with pyridoxine. Full patient dose should be available for the entire treatment period before initiating treatment in all regimen.*

D. Dosage of Pyridoxine (Vitamin B6)			
Weight (kgs)	**Dosage in mg**	**Number of 25mg tablets**	**Number of 50mg tablets**
<5	6.25 mg	½ Tablet 3 times a week, alternate days	-
5.0-7.9	12.5 mg	Half a tablet	-
8.0-14.9	25 mg	One tablet	Half of 50mg tablet
15kg and above	50 mg	Two tablets	One 50mg tablet
Adults	50 mg	Two tablets	One 50mg tablet

TB-LAM is a rapid point-of-care urine dip-stick test that can be performed at the bedside. LAM stands for lipoarabinomannan, which can be detected in urine when it sheds off of the TB cell wall.

GeneXpert is the recommended initial diagnostic test for people with presumptive TB.

TB-LAM SHOULD NOT be used as an alternative test to GeneXpert, but can be performed to help diagnose TB while waiting for GeneXpert test results. TB-LAM cannot detect resistance to rifampicin.

Indications for use of TB-LAM, as an adjunct test to GeneXpert:

- **PLHIV with advanced disease (WHO stage 3 or 4 or CD4 count ≤ 200 cells/mm^3 (or ≤ 25% for children ≤ 5 years old)) with presumed TB**
- **PLHIV that have any danger signs of severe illness:** respiratory rate >30 breaths per minute, temperature >39°C, heart rate >120 beats per minute, unable to walk unaided
- **Currently admitted to hospital**

LF-LAM Negative

TB is not ruled out

- Evaluate the clinical response after 3–5 days of antibiotic treatment, while awaiting GeneXpert results

Clinical improvement

Clinical worsening or no improvement

LF-LAM Positive

TB is likely

- Initiate TB treatment
- Conduct additional investigations for TB and other HIV related diseases as appropriate
- Continue TB treatment even if GeneXpert results come back negative

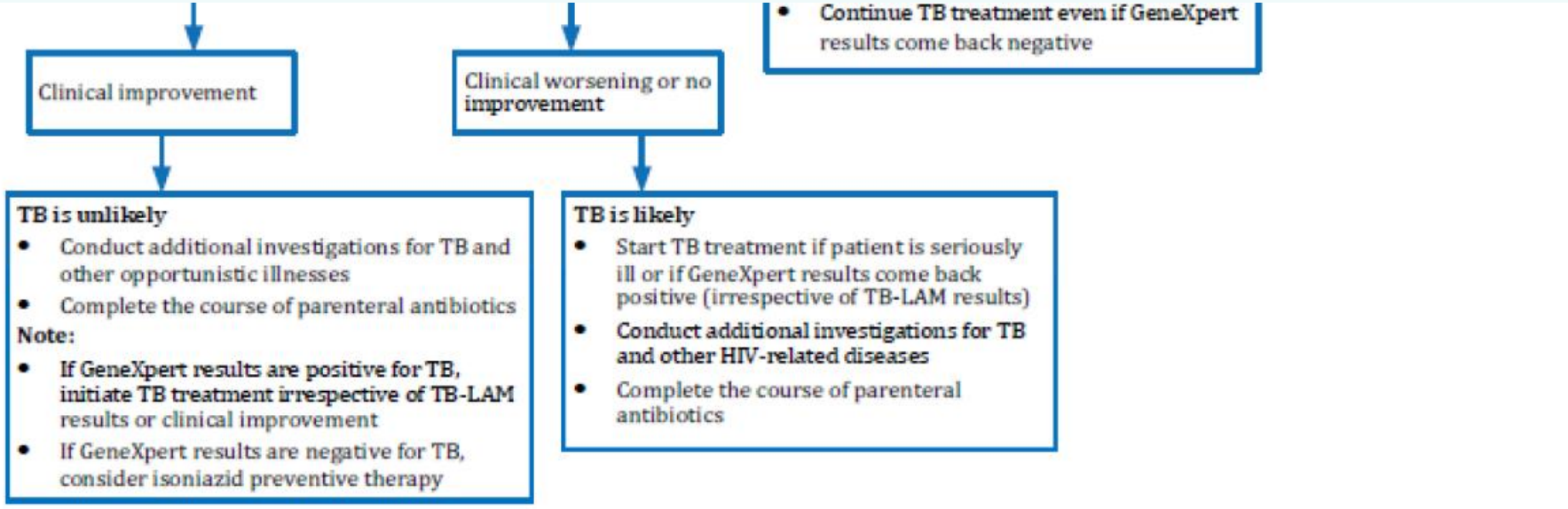


Figure 6.1: TB LAM algorithm

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

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

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

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

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

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

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

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

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

Current Regimen	Age	Recommended substitution
PI/r-based	< 20kgs (above 4 weeks old)	Super-boost LPV/r with additional RTV[4] After completion of TB treatment revert to the recommended first line regimen (ABC + 3TC + LPV/r)
	≥20 kgs	Switch from PI/r to DTG and continue this regimen even after completing TB treatment (give DTG 50 mg BD for duration of rifampicin-containing TB treatment, then reduce to DTG 50 mg once daily 2 weeks after TB treatment is completed). For women and adolescent girls of childbearing potential continue counselling on avoiding pregnancy before use of DTG
EFV-based	Any age	Continue the same regimen for the duration of TB treatment. Consider for regimen optimization after completing TB treatment
DTG-based 20kgs – 35kgs		DTG at x2 standard weight-based BD dosing until 2 weeks after completion of Anti TBs. return to DTG OD 2 weeks after completion of anti TBs
	>35kgs	Give TDF/3TC/DTG FDC am + DTG 50mg pm for duration of rifampicin-containing TB treatment and for an additional 2 weeks after TB treatment is completed, then revert to TDF/3TC/DTG FDC OD