BASIC TUBERCULOSIS (TB) TRAINING MANUAL

PARTICIPANT

2024

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1. AETIOLOGY AND TRANSMISSION OF TB

Module overview:

This module provides an overview of the aetiology and transmission of TB, TB infection, TB disease, and risk factors associated with TB. It serves as a foundation for other topics to follow and it is important that Healthcare Workers (HCWs) have a comprehensive understanding of these basics.

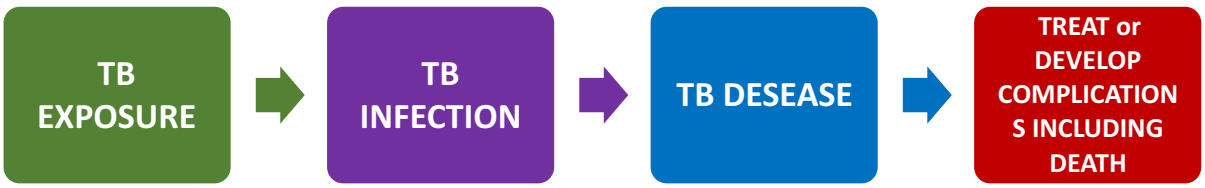
Learning Outcomes:

By the end of this session, participants should be able to:

- Explain the aetiology of TB.
- Describe the transmission and pathogenesis of TB.
- Explain the difference between TB infection and TB disease.
- Explain risk factors and conditions associated with TB.

1.1. Aetiology of TB

The stages of TB



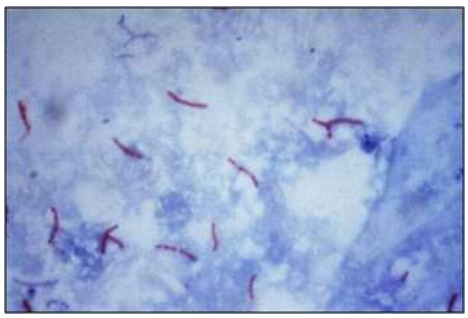
Definition of TB

Tuberculosis (TB) is an **infectious disease** caused by a micro-organism (also referred to as a bacillus), called Mycobacterium tuberculosis (MTB). This bacillus belongs to a group of bacteria, *Mycobacterium tuberculosis complex*. Other agents include:

- *Mycobacterium bovis* (transmitted through contaminated milk and milk products)
- *Mycobacterium Africanum, (causes human TB in West Africa, where it accounts for up to 50% of cases), Macroti (Rodents are reservoir hosts for M. microti)*
- In *rare* situations Mycobacteria other than TB (MOTT) may cause a disease similar to typical TB and is common in HIV infected individuals

Mycobacterium: A large family of bacteria that have unusually waxy cell walls that are resistant to digestion.
The consequences of the cell wall structure are that:

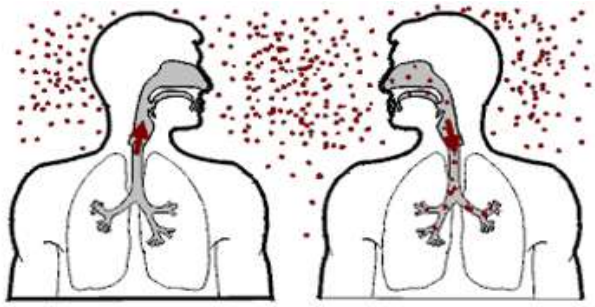
- It protects the bacilli against the host antibodies.



- Commonly used antibiotics (e.g. penicillin) cannot penetrate this waxy layer, therefore there is a need for special TB medicines.
- Special staining methods are needed because with the usual staining methods, the stain cannot penetrate the waxy layer. The mycobacterium is **acid-fast** rod-shaped bacterium. **Acid- fast bacilli (AFB)**: When the mycobacterium is stained, it retains colour even after they have been washed in an acid or alcohol solution. The mycobacteria are usually slow-growing organism.

1.2. TB Transmission

1.2.1. How is TB transmitted?



Exposure to TB bacilli

TB is an airborne infectious disease and is transmitted through airborne route. When a person with pulmonary or laryngeal tuberculosis *coughs, sneezes, talks, laughs or sings,* the small droplets of tubercle bacilli are spread into the air in tiny droplets. Droplet nuclei can also be produced by aerosol which produces investigations such as *sputum induction, bronchoscopy and through manipulation of the lesion*. Other people can breathe in these droplets and become infected.

One cough can produce 3 000 droplet nuclei which can remain suspended in the air for many hours.

TB transmission mostly occurs indoors, in dark and poorly ventilated spaces where the droplet nuclei stay for a long time. Prolonged exposure to the TB bacteria is normally necessary for infection to occur. The large pool of patients with infectious TB leads to a high risk of exposure to the general population. Patients with pulmonary TB present the main source of TB transmission. Close contact and prolonged exposure increase the risk of transmission.

1.2.2. Risk of infection and disease. Factors that determine the likelihood of transmission:

a) Concentration of the bacilli

Bacilli in the index patient

Transmission of TB depends on the number of bacilli expelled into the air:

Talking (0– 210)
Coughing (3500)
Sneezing (1 000 000)

Smear positive patients are more infectious than smear negative patients, due to the high concentration of bacilli. Smear negative patients are expected to have reduced number of bacilli but can also transmit TB bacilli.

b) Length of exposure to TB bacilli

The length of time an exposed person breaths the contaminated air. Close contact and prolong ed exposure increase the risk of transmission. Close contacts of patients with infectious TB including household contacts are at a higher risk of becoming infected with TB.

c) Immune status of the exposed individual

Immuno-compromised patients are at risk of developing TB and progression from latent TB to active TB (HIV, immunosuppressive conditions and drugs, malnutrition, alcohol). The risk of developing TB is higher in children under the age of 5 years, elderly, miners, inmates in prisons, healthcare workers people sharing residential accommodation with TB patients.

d) Environmental factors

Concentration of the organisms in the air, space and ventilation. The concentration of organisms in the air is determined by the volume of space and the ventilation.

1.2.3. Progression of TB disease

Once infected, the progression to active disease is dependent on the immune status of the individual. In those with normal immunity, 90% will not progress to active disease and only 10% will develop active disease. People with suppressed immunity are more likely to develop active TB than those with normal immunity.

1.2.4. Congenital TB

Congenital TB is transmitted from an infected pregnant mother through the placenta, aspiration of infected amniotic fluid, or ingestion of infected material during passage through the birth canal. Mortality from congenital TB is high, estimated at 50%. Early diagnosis and commencement of treatment significantly improve survival.

1.2.5. People at risk of developing TB

Most at risk individuals include:

- **Contacts**
  Household or close contacts are more at risk because of exposure to an index patient.
  - **A household contacts** is someone who shared the same enclosed living space for one or more nights or for extended periods of up to 8 hours during the day with the index patient during the 3 months before the start of current treatment.
  - **A close contact** is a person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods during the day with the index patient during the 3 months before commencement of the current treatment episode
- **Children < 5 years**
- **People living with HIV**
  Infection with HIV increases the risk of progression of recent M. tuberculosis infection and of reactivation of latent M. tuberculosis infection by 5 - 15% annually. It also increases the rate of relapse and re-infection.
- **Healthcare workers, inmates in Correctional Centres, and miners**
- **People with conditions/ on medications which suppress immunity** such as, diabetes mellitus, silicosis, prolonged use of corticosteroids, chemotherapy. In children, the following conditions can increase the risk of progression to TB disease, malnutrition, measles, whooping cough.
- **The elderly >65 years**
- **Smokers**
  Smoking is a risk factor for TB, independent of alcohol use and other socioeconomic factors. The risk is higher in children exposed to passive smoking. Active smoking is associated with recurrent TB disease and death due to TB disease. The possible biological mechanisms for the association between tobacco smoke and TB are that tobacco smoke results in: (a) impaired clearance of mucosal secretions in the tracheo-bronchial tree. This allows the M TB to reach the alveoli; (b) impaired functioning of the pulmonary alveolar macrophages, resulting in lower levels of cytokines being secreted; (c) decreased intracellular tumour necrosis factor- α production leading to impaired intracellular killing of M TB.

- **Alcohol consumption**
  Excessive alcohol consumption (with or without an alcohol use disorder) is associated with three-fold risk of developing TB. Low to medium alcohol consumption is not associated with an increased risk of TB disease. Alcohol use disorders are associated with clinical conditions that may impair the immune system and alcohol has a direct toxic effect on the immune system. Excessive alcohol use is also associated with poor TB treatment adherence and several studies have found higher relapse rate among heavy drinkers and those with alcohol use-related health disorders

1.3. Types of TB Disease

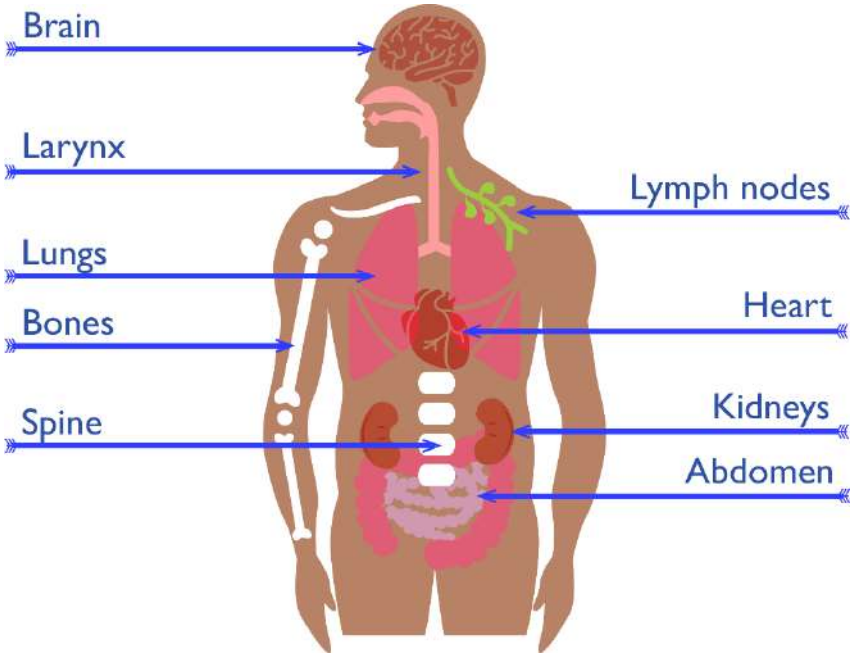
1.3.1. Pulmonary TB disease

Pulmonary TB disease involves the lung parenchyma/tissue. A patient with both a parenchymal lesion in the lungs (PTB) and extra-pulmonary TB is classified as PTB.

1.3.2. Extra-pulmonary TB (EPTB) disease

EPTB disease involves organs other than the lungs. Intrathoracic TB such as mediastinal or hilar lymphadenopathy or pleural effusion without a parenchymal lesion in the lungs, is classified as extra- pulmonary TB. Where several sites are affected, the site representing the most severe form of disease determines the case definition of extra-pulmonary TB.

The organs that are commonly affected in EPTB are: pleural TB (the lining covering the lungs), TB Meningitis (central nervous system), bone and joints, lymph nodes, abdominal TB (where the liver, spleen and the intestines can be affected), and urogenital TB (kidney and bladder, as well as blood).



TB can be further classified as either drug susceptible TB or drug resistant TB:

Drug susceptible TB is a disease caused by MTB strain that is fully sensitive to the first line TB medicines. This means that all first line TB medicines will be effective if they are taken properly.

Drug Resistant TB is a disease caused by MTB strain that is resistant to one or more of the TB medicines. Patients with drug resistant TB are categorised by the resistance pattern of MTB strain.

Types of DR-TB

Type	Definition
Rifampicin Resistant TB (RR-TB)	TB caused by MTB strains that are resistant to Rifampicin, with or without resistance to other TB drugs.
Multi-Drug Resistant (MDR-TB)	TB caused by MTB strains that are resistant to at least both Rifampicin and Isoniazid.
Pre-Extensive Drug Resistant (PreXDR-TB)	TB caused by MTB strains that are MDR/ RR-TB and resistant to any of the fluoroquinolones.
Extensive Drug Resistant (XDR-TB)	TB caused by MTB strains that is MDR/ RR-TB, resistant to any of the fluoroquinolones and at least one of the medications used in the newly recommended regimens including resistance to bedaquiline, clofazimine, delamanid and /or linezolid.
Isoniazid Resistant TB	Resistance to Isoniazid with or without resistance to other TB medicines (excluding Rifampicin).

1.4. TB Infection vs TB Disease

Infection is the invasion of an organism's body tissues by disease-causing agents, their multiplication, and reaction of host tissues to these organisms and the toxins they produce. Infections are caused by infectious agents including bacteria, viruses, parasites, fungi, etc.

Disease is an impairment of normal physiological function affecting all or part of an organism. It is a medical condition, associated with signs and symptoms. It may be caused by factors originally from an external source, such as infectious disease, or it may be caused by internal dysfunctions, such as autoimmune diseases.

Communicable disease refers to a disease resulting from an infection due to pathogenic agents or toxins generated by the infection, following the direct or indirect transmission of the agents from the source to the host. **The pathogenic agent** is also referred to as an **infectious agent**.

Table1.1: Difference between latent TB infection and TB disease

Latent TB infection	TB disease
TB bacilli remain in the body but are inactive	The bacilli actively divide and spread in the body
The individual has no symptoms and signs of TB	The person has symptoms and signs of TB such as a cough, fever, night sweats, weight loss
Cannot spread TB bacilli to other people (not infectious)	The TB disease may or may not be infectious. If PTB and coughing the person will spread the infection to other people
Usually has a positive TB skin test result indicating TB infection	Usually has a positive TB diagnostic test result indicating TB disease
Treatment for latent TB infection must be offered to high-risk groups. This will prevent development of disease	Treatment for TB disease must be started. This will prevent death resulting from TB disease

1.5. Risk factors for progression to TB disease

Factors/ conditions that increase the risk of progression from TB infection to disease include:

- HIV infection
- Immuno-suppressive conditions such as cancers, diabetes mellitus etc.
- Immuno-suppressive therapy such as corticosteroid therapy, chemotherapy etc.
- Silica dust
- Substance abuse (alcohol, tobacco smoking, drugs)
- Low body weight
- Age

2. PREVENTION OF TB

Module overview:

This module provides an overview of tuberculosis prevention in health facilities and in the community, including prevention for people at risk of tuberculosis.

Learning Outcomes:

At the end of this module, participants should be able to:

- Explain TB prevention methods.
- Explain the 7 steps for prevention of TB transmission in health facilities.
- Discuss the hierarchy of infection control measures.
  Explain TB contact investigation.
- Explain actions to be taken during TB outbreak.
- Describe the treatment of LTBI.

2.1. TB Prevention measures in health facilities

Rationale for TB infection prevention and control

TB is a communicable disease and is spread from person to person. The high number of people with undiagnosed, untreated and potentially contagious TB are seen in health facilities and sometimes missed. The high number of HIV positive patients seen in facilities are particularly vulnerable to TB. This creates the potential for high level of nosocomial transmission of TB. It is the responsibility of management to minimise the risk of TB transmission in health facilities. Infection control measures should be established to reduce the risk of TB transmission to general population and healthcare workers. Infection prevention and control measures should be implemented in primary healthcare facilities, hospitals, congregated settings and community

TB prevention measures include:

- Infection Prevention and Control in healthcare facilities
- Contact Investigation; outbreak response
- BCG vaccine
- Treatment of Latent TB Infection (LTBI)

2.1.1. Managerial control measures

Managers provide leadership by providing a culture of safety and advocating for necessary resources to conduct infection control measures. The managerial control provides a framework for the implementation of the infection prevention and control measures. Facility level managerial activities include:

- establishing an infection and control committee for the facility
- appointment of an IPC officer
- conducting facility TB risk assessments annually
- developing and reviewing infection control plan
- monitoring the number of health staff diagnosed with TB monthly
- train and educate health workers on infection prevention and control measures
- ensuring availability of appropriate commodities for TB IPC
- conducting IPC audits to monitor the implementation of TB infection Prevention and control intervention

The TB infection control program should be based on a three-level hierarchy of control measures and include:

- Administrative control measures
- Environmental measures
- Personal protective equipment (PPE)

2.1.2. Administrative control measures

Administrative control measures aim to reduce droplet nuclei containing MTB in healthcare facilities and thus to reduce the exposure of staff and patients. These measures have the greater impact in TB control and should be prioritised.

The seven steps to reduce droplet nuclei and TB transmission in healthcare settings are listed below.

Table 2.1: Seven steps for patient management to prevent transmission of TB

Step	Action	Description
1.	**Screening**	- Early recognition of patients with TB symptoms. - Assign staff member/s to screen patients for TB and COVID-19 symptoms. - All patients presenting with symptoms must be triaged to testing. - Specimens for COVID-19 (if applicable) and TB testing must be collected. - Where available, chest x-rays should be used to screen asymptomatic patients for TB. - Healthcare workers should clinically assess all patients who present with TB symptoms other than cough.
2.	**Educate on cough hygiene**	- Educate patients on cough hygiene and the use of face masks. - Ensure that all patients wear face masks on entry and during the stay in the health facility. - Provide bins for safe disposal of tissues and masks. - Ensure access to hand washing facilities for patients.
3.	**Separation and isolation**	- Establish separate waiting areas for patients who cough. - Separate clients with TB symptoms from other patients. - Separate new patients with TB from patients who are at various stages of TB Treatment in a TB ward.
4.	**Fast-track**	- Place symptomatic patients at the front of the line for services they are seeking to reduce the amount of the time that others are exposed to them.
5.	**Investigate patients with symptoms for TB**	- Collect sputum for testing from all patients with a cough in designated sputum collection area. - Diagnostic tests should be done, onsite (hospital) or referred to the nearest laboratory (PHC).

		- All patients with TB symptoms should be offered provider-initiated counselling and testing. - Laboratory results should be followed up within 2 days.
6.	**Prompt Treatment**	- Appropriate TB treatment should be initiated at the earliest time possible (within 2 days). - ART should be initiated in all HIV/TB co-infected patients.
7.	**Discharge plan**	- For inpatient settings, discharge planning should be conducted jointly with the patient - Linkage with community healthcare workers to conduct comprehensive infection prevention and control home assessment.

Prevention of TB transmission in hospitals

Hospitals are implementing FAST strategy. FAST is a focused approach to stopping TB spread in congregate settings. FAST stands for Finding patients with TB Actively, Separating safely, and Treating effectively. FAST focuses attention on implementing and monitoring the administrative processes and procedures necessary to find and rapidly diagnose unsuspected infectious TB and drug resistant TB patients, so that TB treatment may start within days, not weeks or months of presentation.

- **Finding people with TB actively**

The most infectious people are those with undiagnosed TB. Undiagnosed TB patients present in outpatient/casualty departments and may end up admitted in the wards for other medical/surgical problems. In most cases they wait long periods of time in crowded and poorly ventilated waiting areas. The consulting rooms where they are seen may be poorly ventilated and without any measures in place to prevent transmission of infection.

- **Patients at OPD/Casualty**

Routinely asking patients about TB symptoms, such as cough, fever, night sweats and weight loss can lead to the identification of people with symptoms for testing. Those found to have TB symptoms should be fast-tracked for sputum collection and laboratory testing – TB NAAT. Laboratory results must be followed up to ensure treatment initiation prior to client leaving the facility.

- **In-patients**

Patients admitted should be screened, tested on admission. Results should be followed up within 24 hours.

- **Separate safely**

Whilst waiting for the laboratory results patients with TB symptoms should be educated on cough hygiene which should include the importance of using surgical masks and separation. They must be provided with surgical masks and take their position in the waiting area or where feasible they can wait in a separate adequately ventilated waiting area.

In the hospital wards patients with TB symptoms must be isolated in a side ward or provided with a surgical mask where separation is not feasible.

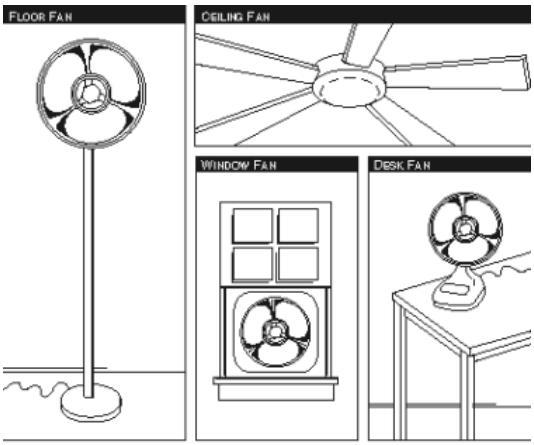
- **Treat effectively**

Effective treatment is the most important step in preventing the spread of TB to others. On receiving the results of the patient, those found to have TB disease must be initiated on effective treatment for DS-TB or DR-TB. Education and counselling of the patients must be conducted on treatment initiation and during follow-up.

2.1.3. Environmental control measures

The environmental controls are second defence in preventing the spread of TB. They are effective if administrative controls are in place. These include:

2.1.3.1. Ventilation (Natural and Mechanical) allows the movement of air through a building so that it is replaced by air from outside.



- **Natural ventilation:** Natural ventilation relies on open doors and windows. There should be adequate number of windows and doors opening to the outside and windows on opposite sides of the room allow good ventilation. Ventilation can be assisted by propeller fans mounted on the ceiling, desk, floor or window.

- **Assisted natural ventilation**

  Fans may be used to assist in air distribution and directing the flow. Fans are inexpensive, increase natural ventilation effectiveness, mix air in a room, reduce concentration of particles, and assist in directing air movement.

- **Mechanical ventilation**

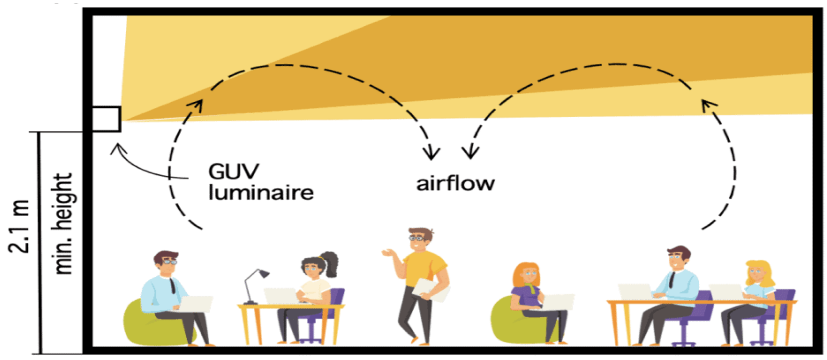
  It is used in areas where there may be high concentrations of infectious droplets. Exhaust ventilation systems allows for exchange of air in the room as well as extraction of the air to the outside and fresh air is drawn into the room. Use in areas where natural ventilation is not feasible or inadequate. It should facilitate air entry into, and exhaust from, the room or area and direct air movement so that aerosols from patient are directed away from others. Directional air flow should be from a “clean” area, across the patient, and to the outside.

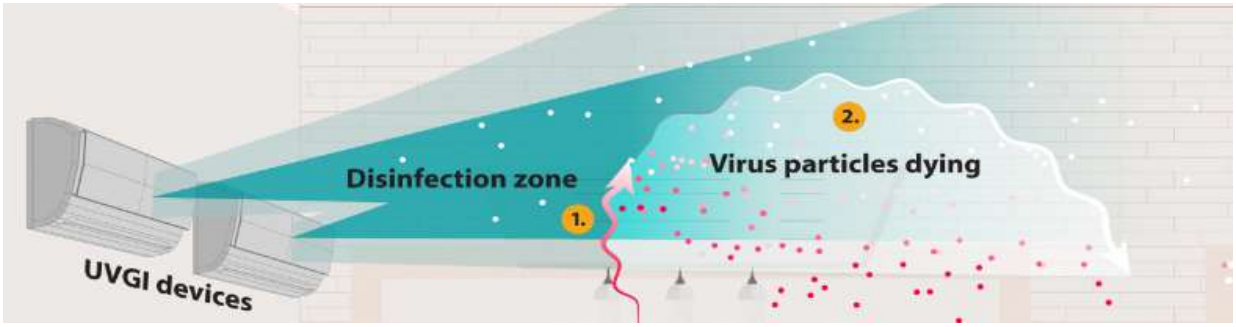
2.1.3.2. Ultraviolet germicidal irradiation (UVGI)

Ultraviolet germicidal irradiation (UVGI) may be used as an adjunctive measure or where natural ventilation is not feasible, UVGI may be a useful alternative. They require ongoing maintenance and monitoring.

The airborne pathogens are killed once they receive an appropriate amount of UV energy. For this to be effective air circulation is important to ensure that the droplets must come into contact with the UV rays in the disinfection zone natural ventilation, fans or other mechanical methods may be considered to facilitate air circulation.

Ultraviolet kills the bacilli. For this to be effective it must come into contact with the rays, therefore circulation of the air is important.





2.1.4. Personal Protective Equipment (PPE)

Personal protection refers to the use of respirators that contain a special filter material to protect the wearer from inhaling the TB bacilli. N95 or FFP 2 are recommended for use in healthcare settings. PPE should be used together with other control measures to protect users against high-risk exposure. Healthcare workers must be trained on the proper use and storage of the respirators.

2.1.4.1. Types of respirators

- **N95 respirator**

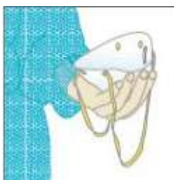
N95 is particulate filtration respirator face piece used for protection against airborne infections such as tuberculosis. It is NIOSH (National Institute for Occupational Safety and Health – part of U.S. Centers for Disease Control and Prevention) certified and has capacity to filter out 0.3-micron particles at 95% efficiency.

- **FFP2 respirator**

FFP2 particulate respirator face piece used for protection against airborne infections such as tuberculosis. It is a conformity standard of Europe. The “filtering face piece” score (FFP) comes from EN standard 149:2001. It has capacity to filter out 0.3-micron particles at 94% efficiency.

2.1.4.2. Donning of the respirator

Healthcare workers must ensure that, the respirators cover the nose, mouth and chin provide a tight seal around the edge.



-Wash your hands using soap and water or clean with hand sanitizer
-Inspect the mask to ensure that it is not damaged
-Cup the respirator in your hand with the nosepiece at your fingertips, allowing the headbands to hang freely below your hand
-Separate the elastic straps

-Position the respirator under the chin with the nosepiece up
-Pull the top strap over the head resting it high at the back of the head.
-Pull the bottom strap over the head and position it around the neck below your ears

Place fingertips of both hands at the top of the metal nosepiece. Mould the nosepiece (using two fingers of each hand) to the shape of your nose.

2.1.4.3. Doffing/ Removal of respirator

- Lift the bottom strap around the neck up and over the head
- Lift the top strap around the crown of your head over
- Make sure not to touch the respirator
- Store the respirator in a marked paper bag

2.1.4.4. Seal check

- Seal check is a procedure conducted to determine if the respirator is properly worn.
- A seal check must be performed by lightly covering the respirator with both hands and forcefully inhaling and exhaling
- If respirator collapses inwards on inhaling without air leaks between face and respirator = Negative seal check
- If respirator expands/ air build up felt on exhaling without air leaks between face and respirator = Positive seal check

2.1.4.5. Use and storage of respirators

A respirator extensively used should be discarded after 7 days. N95 respirators must be stored in a clean, dry, ventilated place. Deterioration of respirator efficiency occurs with humidity, dirt and crushing, therefore the condition of the respirator must be checked before re-use. Respirators are disposed as “soft waste” and do not need to be disinfected before being discarded.

2.1.4.6. Fit testing

Fit testing must be performed on all health care workers to determine which type or size of respirator fits properly.

- It makes use of a noxious substance that is sprayed in a hood covering the head
- If the individual can smell the substance, it means the respirator does not fit well
- If the individual cannot smell the substance, it means the respirator fits well

Once the correct type and size has been determined for an individual, fit testing does not need to be repeated.

2.1.4.7. Surgical masks

Surgical masks are meant to prevent the spread of droplet nuclei into the air by capturing the expelled particles near the source (mouth). They do not provide adequate protection from inhaling infectious droplet nuclei in the air because they are not sealed and have limited filtration capacity. They should be worn by patients who are coughing.

Use of face masks

Table 2.2: Mask vs Respirator

	MASK	RESPIRATOR
Purpose	To reduce transmission	To reduce exposure
Who should wear it	Patients with infectious PTB People with cough	Health facility staff Visitors to the TB isolation wards Community Healthcare workers
Where should it be used	Waiting rooms, consulting rooms and isolation wards During transportation i.e. ambulance, patient transport vehicles or other At home if isolation is not possible, ventilation inadequate	TB isolation wards Sputum collection/ induction areas Other high-risk areas based on the risk assessment During transportation especially when sharing the vehicle with a person who has infectious TB visits to homes of patient with infectious TB

2.2. TB Risk assessment

Risk assessment should be undertaken to identify potential risk areas for infection transmission so that proper IPC measures can be implemented. The TB risk assessment determines:

a) The risk of nosocomial transmission of TB by looking at several factors: –
b) incidence of TB in the community
c) number of patients with TB disease seen at the facility
d) timelines of identification, isolation, testing and treatment of people with TB symptoms
e) evidence of transmission at the facility
f) types of control implemented in the facility
g) The types of administrative, environmental and respiratory protection controls that need to be implemented in the facility.

Risk assessment also serve as a tool for ongoing evaluation of the quality of TB infection control measures and the need to strengthen them. A TB risk assessment for healthcare facilities must be conducted and documented at least annually. The TB risk assessment tool (Annexure 1) may be used as a guide for conducting a risk assessment for a Primary Healthcare facility.

The identified risks from the risk assessments serve as the basis for the TB infection prevention and control plan. Every facility must have a written TB IPC plan based on the risk assessment conducted. The plan must contain information about how the facility:

a) defines employees who are at high risk of occupational TB exposure
b) identifies patients with presumptive TB
c) isolates or controls exposures when a suspected or confirmed TB patient is identified
d) minimises the risk of exposure for employees
e) alerts the employees to hazards
f) screens employees for TB
g) uses and maintains environmental controls implemented to reduce risk of exposure
h) uses respiratory protection
i) trains employees on TB
j) monitors the implementation of the facility TB IPC

2.3. Contact management

TB Contact investigation

It is systematic identification of people with undiagnosed TB disease and TB infection among the people who have been recently exposed to the index TB patient in the household and in other settings where transmission of infection is likely to occur (significant TB exposure). This includes identification, tracing, clinical evaluation, testing and provision of appropriate TB treatment. Household and close contacts of people with active PTB are at increased risk of acquiring infection.

Recent TB exposure: Contact with a person diagnosed with pulmonary TB in the last 12 months. **Significant TB exposure:** Known exposure to a person (adult or adolescent) with pulmonary TB who shared the same enclosed space for one or more nights or for frequent or extended daytime periods during the three months before the index patient starting their TB treatment. Significant TB exposure can occur in any setting, e.g., the household, workplace, place of learning or care.

Objectives of contact tracing

The objectives of contact tracing are to:

- conduct TB testing as an entry point to treatment (treatment of TB disease and treatment of LTBI)
- identify contacts with active TB disease and initiate treatment early to reduce transmission in the communities
- identify those infected with TB and at high risk of developing active tuberculosis for TB preventive treatment to prevent progression to TB disease

Definition of a TB contact

A person who has been in close contact sharing the same environment with the index patient.

Two types of contacts

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

Household contact: A person who shared the same enclosed living space for one or more nights or for frequent or extended periods of up to 8 hours during the day with the index patient during the three months before the start of current treatment

Note: The above definition extends household contacts to include sleep overs. This is an important fact for sexual partners especially HIV positive partners.

Objectives of contact investigation

- to reduce morbidity and mortality due to TB
- to arrest further transmission by early detection of patients with TB
- to prevent future cases of TB in the population by early detection, providing prevention therapy to high-risk contacts:
  a) Children under the age of 5 years
  b) People living with HIV

Benefits of contact tracing

Contact investigation offers an opportunity to:

a) provide individual and family education on TB disease and infection prevention measures
b) conduct interview with the patient promptly to assess the need for urgent contact tracing and investigation

Table 2.3: Determinants of risk of TB infection

Factors that determines the risk of TB infection				
1. Infectiousness of the index patient	2. Closeness and duration of exposure	3. Environment in which the exposure is suspected to have occurred	4. Specific settings presumed to increase the risk of TB transmission such as OPD, general/ TB wards and during sputum inducing procedures	5. Frequent and intense contact of less than 8 hours may be considered to pose similar risk.

Priority contacts

The urgency of contact investigation depends on a number of factors with include:

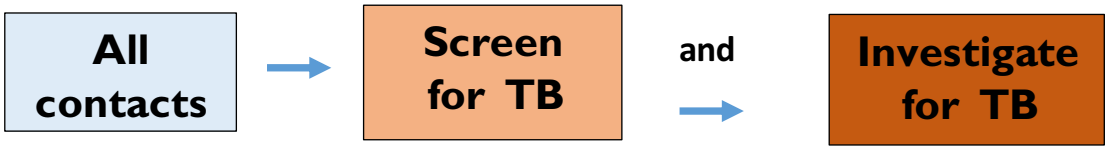
a) **The infectiousness of the index patient**, Where the index patient is "sputum smear-positive" have the highest potential of being transmitters
b) **The immunity of contacts** (children <5 years, immuno-compromised people)

Conducting contact investigation

Household contacts of patients with active TB must be listed in the TB treatment record of the index patient. All contact should be screened. Where available chest x-rays maybe conducted to *screen* for TB. Contacts should be tested for TB, regardless of TB symptoms (Sputum specimen collected for TB NAAT testing). Those diagnosed with TB must be initiated on treatment. Those without TB should be initiated on treatment for latent TB infection, known as TB preventive treatment.

Contact investigation in children under 5 years

Efforts should be made to obtain sputum. If sputum cannot be obtained and the child is asymptomatic, initiate TPT. TST is not required in well asymptomatic children.



Records used for contacts

- **TB Treatment record (index patient)**

Contacts must be documented at the back of the patient TB Treatment Record (GW20/12).

- **TB Identification register**

All contacts investigated for TB should appear on the TB Identification Register. People eligible and started on TPT must be documented in the TB Identification Register.

- **TB treatment record (Newly diagnosed patient)**

Those that are diagnosed with TB, a patient folder must be opened.

Confidentiality, during contact investigations must be maintained. Legal and ethical issues can be resolved by obtaining informed consent for disclosure of information from the patient. Refusal to grant consent pose threat to public health and requires documentation and legal opinion to be sought for determining acceptable interventions. Obtain consent from the patient to disclose to the household and close contacts.Contact household and close contacts through phone call, use of contact slip and conducting home visits. Interview the contacts, inform them about possible exposure to TB and the need for screening and testing for TB disease. Obtain additional information about possible risk of exposure. Conduct medical evaluation. Medical evaluation includes symptom review, sputum examination, skin test and chest X-ray.

Contact diagnosed with TB should be treated for active TB disease. Contacts with no active TB disease should be treated for Latent TB infection (TPT). Determine if investigation needs to be expanded based on evidence of disease transmission and additional contacts and settings identified. Expand contact screening until no evidence of new transmission.

2.4. TB outbreak response

TB outbreak is an observation of more TB patients than expected in a geographic area or population during a particular time, with evidence of recent transmission of MTB among those patients. It involves multiple TB patients with several overlapping contacts.

TB outbreak response is a process of investigating, planning and implementing interventions to manage the outbreak following suspicion of an outbreak.

TB outbreaks can be detected through laboratory data analysis and geo-mapping of confirmed TB cases, routine TB data analysis at facility to monitor trends in TB notifications, routine review of the contact investigation results, and observations by community members.

Confirming an outbreak involves reviewing clinical findings and laboratory results for each case, to confirm that they had TB. Where inconsistencies exist between clinical findings for cases with laboratory results, further information may be required to confirm TB disease.
Epidemiologic links among cases assist in confirming an outbreak. These are shared characteristics between index cases and contacts that explain where and when TB could have been transmitted between them. Some contact investigation findings are evidence of recent transmission, which can indicate a potential TB outbreak.

The goal of TB outbreak response is to interrupt ongoing transmission of MTB. Contacts can be exposed to more than one index case or can be interrelated through multiple connections. Outbreak response requires a multi-sectoral response including partners and stakeholders, a robust communication strategy, collaboration with community leadership and financial resources. The provincial TB Programme Manager after consultation with CDC district coordinator and the district management team can declare a TB outbreak and initiate an outbreak response.

2.5. BCG

Bacille Calmette-Guerin (BCG) is a vaccine for TB disease. It is a live attenuated form of Mycobacterium Bovis (part of MTB complex) which provides children with a degree of protection against disseminated and severe forms of TB. In South Africa, it is given as part of Expanded Programme on Immunisation (EPI) schedule. BCG is given immediately after birth or in the first year of life and not recommended after one year.

2.5.1. BCG AND HIV

It is recommended that asymptomatic HIV exposed neonates should be given BCG. It should not be given to symptomatic HIV exposed neonates born to mothers with TB. Children given BCG should be closely monitored for disseminated BCG disease.

2.5.2. BCG and TPT in infants

- Defer BCG vaccination in infant starting TPT to after TPT completion since TB drugs impair the effect of live BCG vaccine.
- For HIV-positive infants who have just had BCG and are not TB-exposed, TPT should be deferred for 14 weeks as INH impairs the effect of live BCG vaccine.

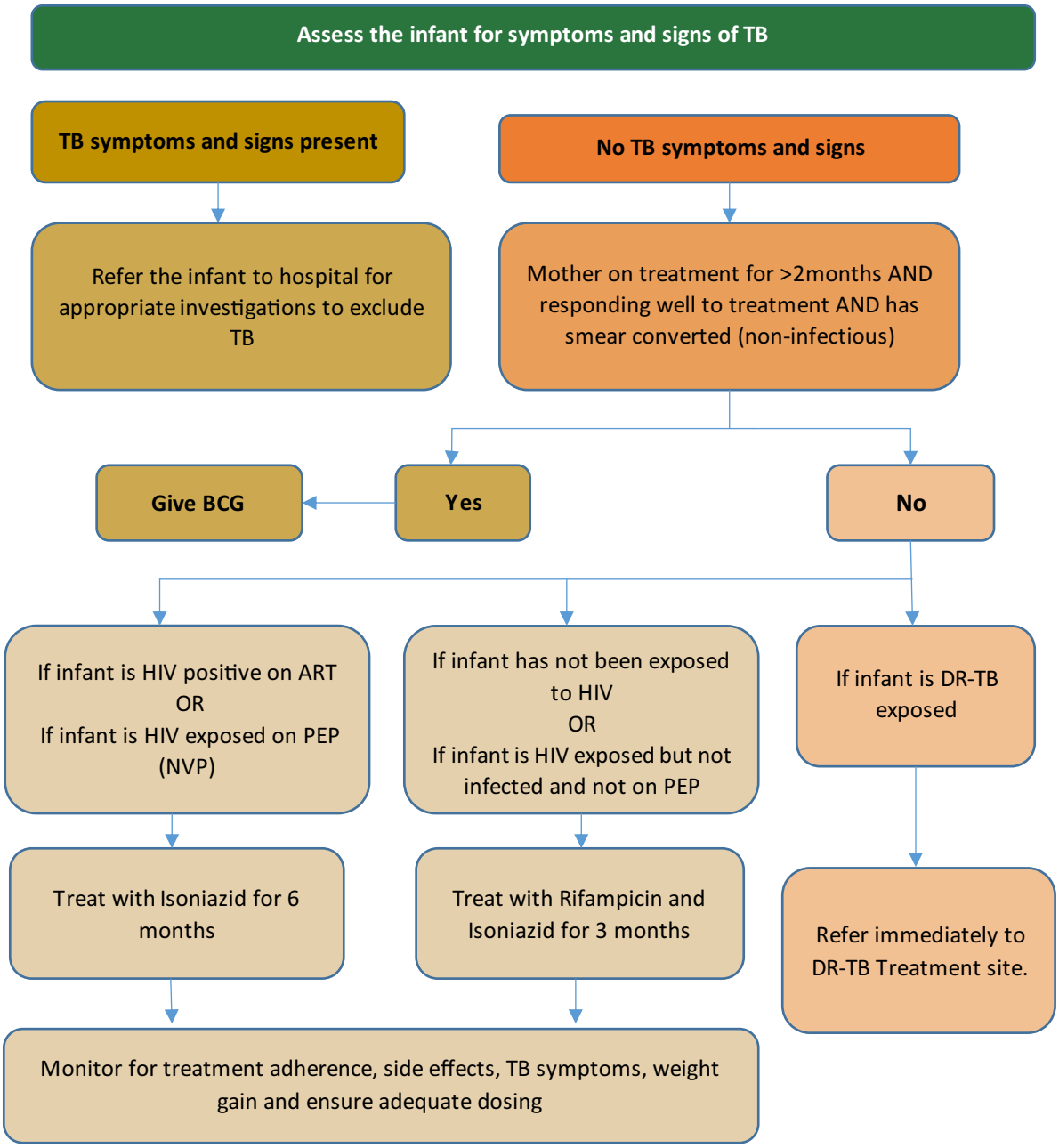
Management of infants born to mothers with TB or with significant TB exposure
Infants have a high risk of developing severe or disseminated TB if exposed to TB and not treated. TB exposed infants are those:

- born to mothers diagnosed with TB in the last two months of pregnancy, at birth or after birth, or
- born to mothers who are still infectious (smear/ culture positive) at the time of birth, or
- born to mothers who are not clinically responding to TB treatment at the time the baby is born.

Infants may also be exposed to another person with TB inside or outside the household. In infants, TB disease should be excluded through clinical evaluation of the baby, including respiratory and abdominal examination; collection of an appropriate specimen for TB NAAT testing or culture. CXR should be done where required. Abdominal ultrasound may be required in case of abnormal clinical findings such as abdominal distension or hepatomegaly.

The infant should be managed according to the algorithm outlined in the figure below. Unwell TB- exposed neonate or infant should be referred immediately for further investigation given the high risk of TB and non-specific clinical presentation of TB in infants.
BCG vaccination should be deferred in an infant starting treatment for TB infection until treatment is completed since TB drugs impair the effect of live BCG (M. bovis BCG) vaccine.

Figure 1: Algorithm to assess the infant for symptoms and signs of TB



- The clinical assessment for TB must include examination of lungs, abdomen and central nervous system and take into consideration low birth weight/prematurity.
- BCG must be given two weeks after completion of TB infection in all TB exposed infants.
- If TB disease is diagnosed, TB treatment must be started, and BCG given 2 weeks after completion of treatment .

2.6. Treatment of Latent TB Infection (LTBI)

Table 2.5: What is Latent TB Infection?

	Latent TB Infection	Subclinical TB disease	Active TB Disease
TST	Positive	Positive	Usually, positive
TB NAAT	Negative	Usually, negative	Positive or negative
Culture	Negative	Intermittently positive	Positive
Infectious	No	Sporadically	Yes
Symptoms	None	Mild or none	Mild to severe
Preferred treatment	TB preventive treatment	TB treatment	TB treatment

The table above depicts the changes in tests, symptoms and infectiousness as the patient progresses from latent TB infection to active TB disease.

Latent TB Infection (LTBI) is a condition where a person is infected with TB mycobacteria but does not become sick or develop TB disease. This happens when the body can fight and contain the infection. The bacilli remain dormant and can be reactivated over time or when the immune system is suppressed. As a result, the person will not have TB symptoms and cannot spread the infection to others. The only evidence of infection is a positive TB skin test. Treating LTBI reduces the risk of developing TB disease in high-risk groups. It is much easier to treat TB infection than disease because the bacillary load is much lower and requires fewer medicines.

Treatment of LTBI

Treatment of LTBI also known as TB Preventive Treatment (TPT), consists of a course of one or more anti-tuberculosis medicines given with the intention to prevent the progression from TB infection to active TB disease. Treatment of LTBI should be offered to all people after **significant TB exposure** (regardless of age and HIV status) and those who are **immune compromised (regardless of known exposure),** e.g. PLHIV, people with silicosis, after TB disease has been ruled out.
NB: TPT does not prevent TB infection.

2.6.1. Who is eligible for TPT?

HIV Positive

- All HIV-infected non-pregnant adults, adolescents and children who have not completed a course of TPT before, irrespective of exposure.

Contacts

- Child contacts irrespective of HIV status and age
- Adolescent and adult contacts irrespective of HIV status
- Inmates who are contacts in Correctional Services facilities

People living with silicosis

Healthcare workers

2.6.2. Exclusion criteria

The following patients are not eligible for TPT

- Patients with confirmed TB disease or on TB treatment
- Patients with symptoms and signs of severe peripheral neuropathy
- People with active acute or chronic liver disease
- Patients with a history of adverse reaction to any of the medications used for TPT
- Patients with alcohol use disorders (excessive alcohol use) and unwilling or unable to scale down use:
  a) For men: more than 5 standard drinks on any day or 15 drinks per week
  b) For women: more than 4 standard drinks on any day or 8 drinks per week

Table 2.4: Estimated standard drink for alcohol

Type of alcoholic drinks	Examples	Standard drink
Beer/wine coolers	≈5% alcohol	360ml
Malt liquor	approximately≈7% alcohol	240-270ml
Cider	about ≈ 6% alcohol	300ml
Wine	Table wine is≈ 12% alcohol	150ml
	Fortified wines e.g. sherry or port	90-120ml
Spirits and liqueur	whiskey, gin, vodka, or brandy≈ 40%	45ml
	Cordial or aperitif	60 -90ml
	A shot is filled to about 45ml	45ml

Treatment should be deferred in patients diagnosed with TB disease, until completion of treatment. Patients with acute liver disease should be assessed for eligibility after treatment completion and liver function test back to normal.

Initiation of TPT should be deferred in all pregnant women until after delivery. Pregnant women should be screened for TB at every visit.

Table 2.5: Excluding TB before TPT initiation

	Old guidelines	New guideline
5 years and older	Exclude TB through: - Symptom screen - If negative screen, initiate TPT	Exclude TB through: - Symptoms screen - Chest x-ray screening only if available on site* - TB NAAT testing
Under 5 years	Exclude TB through: - Symptom Screen - If negative screen, initiate TPT	Exclude TB through: - Symptom screen - TB NAAT testing if a sample can be obtained for testing - If no TB/asymptomatic, initiate TPT
* Chest x-ray screening is not recommended for children under 15 years TB NAAT testing, TST and chest x-rays are not a requirement for TPT initiation in children under 5 years.		

2.6.3. Treatment options for treating LTBI:

- 3HP: 3 months of Isoniazid and rifapentine given once **weekly**
- 3RH: 3 months of **daily** rifampicin and Isoniazid
- 6H: 6 months of **daily** Isoniazid
- 12H: 12 months of **daily** Isoniazid
- 4R: 4 months of **daily** rifampicin

The 4-month rifampicin regiment can only be considered for use in people who cannot tolerate Isoniazid. Where possible shorter TPT regimens should be prioritised.

Figure 2.1: General algorithm for provision of TB preventive therapy in HIV negative individuals

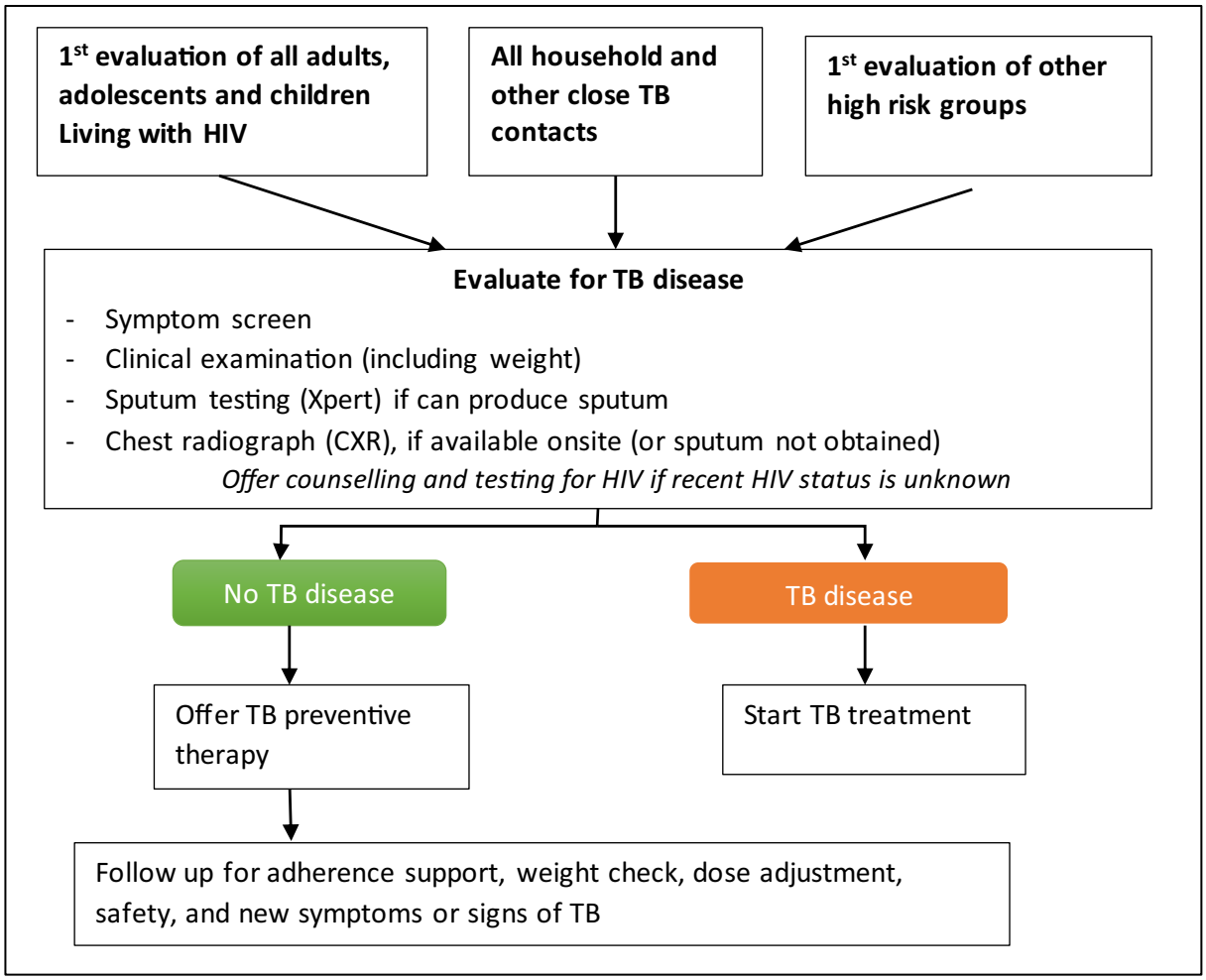
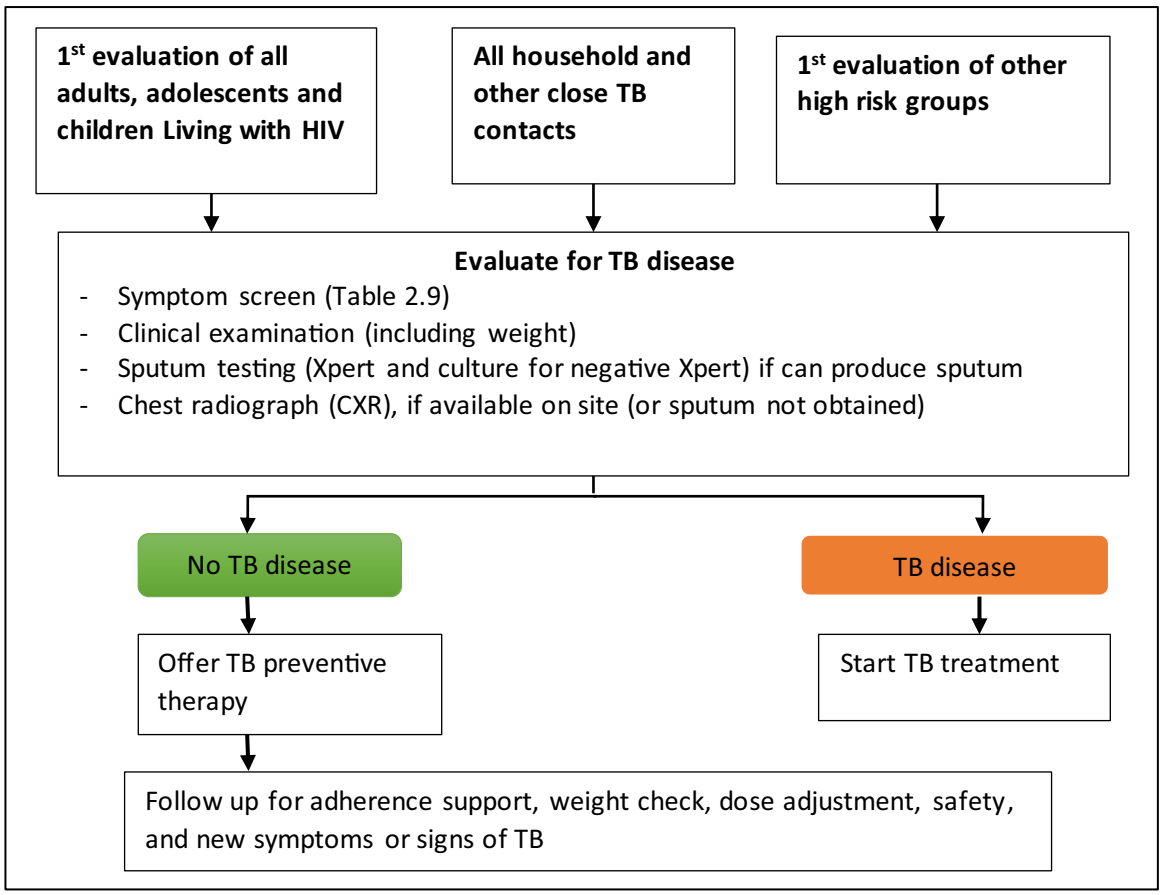


Figure 2.2: General algorithm for provision of TB preventive therapy in HIV positive individuals



- If a CXR has already been done recently in a child who presented with no signs or symptoms, do not repeat the CXR.
- Tests of TB infection (tuberculin skin test/TST) are not required to initiate TPT in children who are TB contacts.

2.6.4. TPT eligibility in children < 25kg

- All children living with HIV (irrespective of significant TB exposure)
- New TB exposure irrespective of history of TPT or TB treatment
- Infants born to mothers diagnosed with TB:
  - in the last two months of pregnancy or at/after birth, or
  - who are still infectious (smear positive), or
  - who are not clinically responding to TB treatment at the time the baby is born, are classified as TB exposed

2.6.5. Exclusion of TB disease in children <25kg

Exclusion of TB disease in infants:

- Clinical evaluation - respiratory and abdominal examination
- Gastric aspirates for TB NAAT, mycobacterial culture, and CXR
- Abdominal ultrasound is needed in case of abnormal clinical findings (distension or hepatomegaly)

2.6.6. Exclusion of TB disease in older children <25kg

Symptom screening

Table 2.6 TB symptom screen

TB symptom screen (adolescents/adults)	TB symptom screen (infants and children)
Current cough of any duration	Current cough
Persistent fever for 2 weeks or more	Persistent fever for 2 weeks or more (irrespective of treatment for < 5 years)
Unexplained weight loss of >1.5kg in a month, or failure to gain weight in pregnant women	Fatigue/less playful
Drenching night sweats	Weight loss or failure to thrive

TB testing amongst children

Sputum testing (TB NAAT) should be attempted in older children who can expectorate spontaneously, and in any other children who can expectorate spontaneously. If a young child can expectorate sputum, a sample collection should also be attempted. CXR is a valuable tool to rule out TB disease in children. The absence of a CXR should however, not pose a barrier to treatment initiation in well children. In a well-child with no TB signs or symptoms, a CXR is therefore not required to initiate treatment. Clinical follow-up remains important. Test of TB infection (TST) is not a requirement for initiating treatment for TB infection.

2.6.7. TPT regimens for children <25kg

There are three potential regimens for children: 3RH and 6H. The choice depends on the child's weight, HIV status or HIV exposure (maternal HIV) status:

In HIV-negative children <25kg, the priority regimen is 3RH

- In children living with HIV and on DTG (dolutegravir) containing ART

6H to avoid drug-drug interactions with ART

- In infants born to HIV-positive women (HIV-exposed but HIV-negative infants) on nevirapine

6H is the priority regimen as rifampicin lowers nevirapine levels below efficacy

All children including infants require pyridoxine (vitamin B6) for the duration of their TPT as follows: children <5 years 12.5mg and child ≥5 years 25mg, once daily. Lack of pyridoxine access should not be a barrier to receiving TPT.

TPT regimen options dosage tables

Table 2.7: Daily dosage for 3RH in children <25kg

Child's weight	RH (Daily) fixed dose combinations		Duration
	75/50	If dispersed in water	
2-2.9	½ tablet	5ml	3 months
3-3.9	¾ tablet	7.5ml	
4-5.9	1 tablet	10ml	
6-7.9	1 ½ tablet	15ml	
8-11.9	2 tablets	20ml	
12-15.9	3 tablets	30ml	
16-24.9	4 tablets	40ml	
≥25	Use adult formulations and doses		

Table 2.8: Recommended daily dosages for the 6H regimen amongst children < 25kg

Weight band (kg)	Daily INH 100mg tablet	Duration
2 – 3.4	¼ tablet	6 months
3.5 – 4.9	½ tablet	
5 – 7.4	¾ tablet	
7.5 – 9.9	1 tablet	
10 – 14.9	1 ½ tablet	
15 – 19.9	2 tablets	
20 -24.9	3 tablets (or one 300mg tablet)	
≥25	Use adult formulations (maximum dose 300 mg per day)	

2.6.8. TPT regimens for children, adolescents and adult ≥ 25kg

HIV negative children, adolescents and adult ≥ 25kg

There are currently four potential regimens for children, adolescents and adults **≥ 25kg,** 3HP, 3RH, 6H or 12H. The short course 3HP regimen should be prioritized if possible. If 3HP is not available for HIV- negative children ≥25kg, adolescents and adults, use 3RH.

HIV positive children, adolescents and adult ≥ 25kg

For adults, adolescents and children ≥25kg living with HIV and initiating dolutegravir -containing ART, 12H is preferred.

For PLHIV who are virally suppressed (VL, <50 copies/mL in the last 6 months,) on a dolutegravir- containing regimen, 3HP is preferred.

2.6.9. TPT regimen options for pregnant and breastfeeding women

For HIV negative, pregnant and breastfeeding women, there are two regimen options: 3RH or 6H

- Give TPT once TB disease has been excluded regardless of CD4 cell count

Pyridoxine (vitamin B6) 25mg daily should be added for the duration of treatment irrespective of HIV status.

TPT Regimen options dosage options

Table 2.9: Recommended regimen for 6H in PLHIV on ART

Drug	Dosage*	Number of tablets (daily)	Duration
Isoniazid	300mg	1	6 months
	Or 100mg	3	6 months

- If 300mg tablets are not available, use 100mg

Table 2.10: Recommended regimen for 12H in PLHIV on ART

Drug	Dosage*	Number of tablets (daily)	Duration
Isoniazid	300mg	1	12 months
	Or 100mg	3	12 months

Table 2.11: 3HP regimen ≥ 25kg

Body weight (kg)	Rifapentine 150mg tablets (weekly)	Isoniazid 300mg tablets (weekly)	Duration
25-29.9kg	**4**	**2**	12 weeks (3 months)
30-49.9kg	**6**	**3**	12 weeks (3 months)
>50kg	**6**	**3**	12 weeks (3 months)

How to take 3HP

- 12 weekly doses must be taken at once on the same day every week for 12 weeks
- If a dose is missed:
  - missed dose should be taken as soon as they remember within 3 days
  - continue the next dose as scheduled or
  - start a new weekly schedule on the day you took the missed dose.
- A course is considered completed if all doses are taken within 16 weeks (11 doses can be counted as complete although not ideal)

Table 2.12: 3RH for adult, adolescents and children ≥ 25kg

Body weight	RH(150,75)	RH(300,150)
	Number of tablets (daily)	Number of tablets (daily)
25-37kg	2 tabs	
38-54kg	3 tabs	
55-70kg		2 tabs
>70kg		2 tabs

Table 2.13: Summary of TPT regimen options by patient type

PATIENT CATEGORY		WHAT TO DO	REGIMEN
ADULTS AND ADOLESCENTS INCLUDING	HIV-POSITIVE	**PLHIV:** Test for TB regardless of ART status and give TPT once TB disease is excluded. If newly diagnosed with HIV, start ART immediately and TPT within 2 weeks.	3HP* or 12H
		Post TB treatment: Offer TPT to all PLHIV ≥25 kg after successfully completing treatment for TB disease, after active TB disease has again been excluded.	
		Previously treated with TPT: If re-exposed to any close contact with TB, retest for TB and give TPT once TB disease has been excluded.	
	HIV-NEGATIVE	**Contacts:** Evaluate all HIV-negative adults, adolescents and children ≥25kg in close contact with people diagnosed with TB and start TPT once TB disease has been excluded.	3HP, 3RH or 6H
		Evaluate all HIV-negative **at-risk groups** (on anti-TNF treatment, on dialysis, preparing for organ or haematological transplant, or with silicosis). Once TB disease is excluded, start TPT.	
		Evaluate HIV-negative adults and adolescents who **previously received TPT**, if re-exposed to a close contact with TB and start TPT once active TB has been excluded.	
CHILDREN <25KG	HIV +VE	Evaluate all children older than 14 weeks of age living with HIV for TB and start TPT once active TB has been excluded. ART should be started immediately if newly diagnosed with HIV. TPT should be started within 2 weeks of ART initiation.	6H**
	HIV-NEGATIVE	Evaluate **HIV-negative children in close contact** with a TB patient and start TPT after active TB disease has been excluded.	3RH
		Test other **HIV-negative at-risk children** (weakened immune system e.g., cancer, autoimmune diseases, transplant patients on immunosuppressive drugs, receiving dialysis, or inherited immunodeficiency) for TB and start TPT once active TB disease is has been excluded	

*For adults, adolescents and children ≥25kg *initiating* a dolutegravir-containing ART regimen, 12H is preferred. For PLHIV who are virally suppressed (VL<50 VL copies/mL) on a dolutegravir-containing regimen, 3HP is preferred.

**In children <25kg initiating a dolutegravir-containing ART regimen, 6H is preferred.

Once the dolutegravir levels from the DOLPHIN-2, DOLPHIN-kids and TBTC Study 35 trials are available, 3HP will likely be the preferred option in all PLHIV. If 3HP is not available, use either 6H (children<25kg) or 12H (adults, adolescents and children ≥25kg).

Taking the meds - advice for the patients and caregivers:

- 3 RH: given on an empty stomach (before a meal).
- Isoniazid regimen only (6H or 12 H): give on an empty stomach (before a meal). Isoniazid is best absorbed on an empty stomach; there is an up to 50% reduction in peak concentration with a fatty meal.
- 3 HP: give with a meal or directly after a meal (rifapentine is better absorbed with food).

All patients starting ART, or already on ART, and who have **not yet received TB Preventive Therapy (TPT)** should be considered for TPT. Prior to initiating TPT, active TB should be ruled out by screening for TB symptoms. A TST is not required prior to starting TPT. TB testing strategies will vary by age as younger children cannot spontaneously expectorate sputum.

- In well children without symptoms, neither sputum testing nor CXR are therefore requirementsto start TPT.
- Sputum testing should be attempted in children who can expectorate spontaneously (typically > 25kg), but if they are well (without symptoms) and unable to expectorate, they should start TPT, even if no CXR or sputum testing is available.

Treatment of latent TB infection with INH (IPT) in child contact.

The recommended dose of Isoniazid in children is INH10mg/kg/day. The maximum daily dose of INH must not exceed 300mg. The table below shows the recommended dose per wait band.

Children should be weighed at every visit and dosages adjusted based on actual weight to prevent under- or overdosing.

Adding pyridoxine (vitaminB6)

Patients receiving TPT should be offered pyridoxine (vitamin B6) for the duration of their TPT: 25mg/day if 5 years or older, 12,5mg/day if younger than 5 years of age. Lack of pyridoxine supply should not be a reason to withhold or postpone treatment.

2.6.10. Education and counselling of eligible individuals

Patient education should cover the following areas:

- What is TB exposure and infection?
- Why is it important to treat TB infection?
- Who must be treated for TB infection?
- What are the benefits and risks of taking treatment for TB infection?
- What are the treatment options for TB infection and the duration?
- The importance of adhering to treatment.
- How and when to take their treatment?
- How to administer the treatment to a child for a parent/ caregiver?
    a) 3 RH: given on an empty stomach (before a meal)
    b) Isoniazid regimen only (6H or 12 H): give on an empty stomach (before a meal). Isoniazid is best absorbed on an empty stomach; there is an up to 50% reduction in peak concentration with a fatty meal.
    c) 3 HP: give with a meal or directly after a meal (rifapentine is better absorbed with food)
- Possible side effects such as unexplained loss of appetite, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools, and jaundice.
- What to do when the patient experiences side effects?
- Infection control, including cough hygiene and adequate ventilation.
- Undesirable effects of using alcohol and smoking while on treatment.
- Symptoms of TB and what to do when they experience them.

2.6.11. Follow-up visits

Individuals may be monitored monthly, 3-monthly, or 6-monthly depending on the duration of treatment. For individuals with comorbidities, try to align appointments with other scheduled chronic disease or ART visits to avoid individuals making multiple visits for care.

- TB symptom screening must be conducted at each visit. If symptomatic, investigate for TB.
- Provide on-going counselling and education.
- Monitor adherence (including pill count and missed appointments).
- For poor treatment adherence or treatment interruption, ask about the possible reasons and counsel the individual or parent/guardian.
- Assess individual for side effects if any are present manage them.
- People who are on long-term treatment (6 and 12 months) can be enrolled on Centralised Chronic Medicine Dispensing and Delivery (CCMDD) to receive treatment through that mechanism as follows:
    a. Newly diagnosed HIV patient that has completed the first 6 months of ART with a VL <50 copies/ml
    b. Contacts of people with confirmed TB who have completed 2 months of treatment
    c. People with confirmed Silicosis who have completed 2 months of TPT
- People on CCMDD must be advised to present to facilities if they develop TB symptoms, experience side effects or if their health deteriorates whilst on treatment.
- Clinical monitoring must be conducted at 3 or 6 months and during the last month of treatment, at which point the treatment outcome will be documented.
- People on short regimen (3 and 4 months) will benefit from multi-month dispensing (MMD). They may be followed up monthly or at 3 months depending on their preference to ensure patient centric care, they must be advised to present to facilities if they develop TB symptoms, experience side effects or if their health deteriorates whilst on treatment.
- People at high risk of treatment interruption must not be enrolled on CCMDD or MMD.

2.6.12. Adverse Events (AEs)

While most of the AEs are minor and occur rarely, major adverse events may occur which may require urgent attention even stopping treatment. Patients should be educated about side effects and what to do should they occur. The table below shows the management of common side effects.

Table 2.14: Management of common adverse events

Adverse event	Drug(s) responsible	Signs/symptoms	Management
Peripheral neuropathy	Isoniazid	Burning pain, pins/needles, or numbness of feet worse at night	- Increase B6 (pyridoxine) from 25mg to 100mg daily until symptoms disappear. - If not better with treatment, or worsens, then H should be discontinued immediately. - Consider rifampicin only alternative treatment regimen.
Hepatotoxicity	Isoniazid(H), Rifapentine(P), Rifampicin (R)	Nausea, vomiting, abdominal tenderness, discomfort near the ribs on the right upper abdomen, jaundice (yellowing of skin and whites of the eyes) Signs: Hepatic enlargement, increased LFTs	- Stop Isoniazid and rifampicin or rifapentine immediately. - refer the individual to the hospital/medical officer immediately for further evaluation.
Gastrointestinal Uncommon at recommended daily doses	Isoniazid(H), Rifapentine(P), Rifampicin (R)	Nausea, vomiting, diarrhoea	- Rule out other causes. - Conduct liver function tests to rule out drug-induced hepatic dysfunction. - Continue treatment based on severity of symptoms. - Treat symptomatically (if no other cause is found.
Flushing reaction	Isoniazid	Flushing and/or itching of the skin with or without a rash, hot flushes, palpitations, headache Signs: increased blood pressure	- Reassure individual and inform about avoiding tyramine and histamine-containing foods (e.g., tuna, cheese, red wine) while receiving Isoniazid. - Flushing is usually mild and resolves without treatment If flushing is bothersome to the individual, an antihistamine may be given to treat the reaction.
Mild itching rash	Isoniazid(H), Rifapentine(P)	Mild rash and itching	- Treat with antihistamine and topical steroid creams.
Hypersensitivity uncommon usually occurs 3 - 7 weeks after initiation of treatment	Isoniazid(H)	hives (raised, itchy rash) fever (may occur)	- Discontinue treatment until the reaction resolves.
Hypersensitivity reaction occurs after the first 3 to 4 doses and begins approximately 4 hours after ingestion of medication	Rifapentine(P)	flu-like symptoms, fever, headache, dizziness, shortness of breath, wheezing, nausea, muscle and bone pain, rash, itching, red eyes, hypotension, or shock	- If mild reaction e.g., rash, dizziness, fever: continue treatment and manage the AEs (adverse events). - If severe reaction e.g., thrombocytopenia (low platelet count) or hypotension, discontinue treatment and refer to hospital.

2.6.13. Drug-drug interactions

- Daily Rifampicin plus Isoniazid for 3 months (3RH) should not be given to infants and children on protease inhibitors (PI) or nevirapine-based ART due to drug-drug interactions.
- Rifapentine and INH (3HP) should not be offered to ART-naïve individuals starting Dolutegravir containing ART due to lack of evidence at this stage. 3HP should be deferred until individuals have **been on** ART with a dolutegravir containing regimen until virally suppressed.

Table 2.15: Common Drug-Drug Interactions

TPT Drug	Drug-Drug interaction	Recommendation
Rifampicin decreases the levels of:	Dolutegravir	Treat with Isoniazid
	Efavirenz	Treat with Isoniazid
	Protease Inhibitors e.g., Lopinavir/Ritonavir	Treat with Isoniazid
Rifapentine decreases the levels of:	Protease Inhibitors e.g., Lopinavir/Ritonavir	Treat with Isoniazid
	Nevirapine	Treat with Isoniazid
	Oral and Implantable contraceptives	Use Barrier method Offer Injectable contraceptive method
	Dolutegravir	Treat ART naïve PLHIV with Isoniazid

Treatment interruption and discontinuation

- People who are initiated on the daily Isoniazid monotherapy (6 - 12month regimen) who interrupt treatment should be categorised as follows:
  a. interrupted treatment for less than 2 consecutive months
  b. interrupted treatment for more than 2 consecutive months
  c. interrupted treatment for a second time regardless of duration of interruption, despite adherence counselling
- People who are initiated on the shorter regimens (3 - 4-month regimens) who interrupt treatment should be categorised as follows:
  a. interrupted treatment for less than 4 consecutive weeks
  b. interrupted treatment for more than 4 consecutive weeks
  c. interrupted treatment for a second time regardless of duration of interruption, despite adherence counselling

2.6.14. Missed doses

Patients should be educated on what to do when they miss doses. The table below gives guidance on how missed doses should be managed.

Table 2.16: Management of individuals who miss doses of treatment

Duration of interruption	Management
If one dose is missed	- The individual should take the missed dose as soon as they remember within the same day - If the day's dose is missed, take the next scheduled dose and continue with the regular schedule. Do not take two doses on the same day - For the weekly doses, take the missed dose as soon as they remember, if this is on the following day, continue the next doses on the new day
If treatment is interrupted for less than 4 weeks for a short regimen or less than 2 consecutive months for a longer regimen	- Enquire about the reasons for treatment interruption - Address individual's concerns - Counsel the individual on the importance of adherence. - If this is the first interruption and person commit to taking treatment. a) Screen clinically for TB symptoms b) Conduct investigations to exclude TB if signs and symptoms of TB are present c) If asymptomatic and no signs of TB disease, continue treatment to complete the remaining doses
If treatment is interrupted for more than 4 weeks for a short regimen or more than 2 consecutive months for a longer regimen	- Enquire about the reasons for treatment interruption - Address individual's concerns - Counsel the individual on the importance of adherence - If this is the first interruption and person commit to taking treatment. a) Screen clinically for TB symptoms b) Conduct investigations to exclude TB if signs and symptoms of TB are present **c)** If asymptomatic and no signs of TB disease restart treatment and referred to relevant health workers for additional support (i.e., psychologist, dietitian, social worker, etc.)
If treatment is interrupted for a second time regardless of duration of interruption and despite adherence counselling	- Do not consider for treatment

2.6.15. Patient categorisation and treatment outcomes

Patients offered TPT may be categorised either as new or previously treated as described in Table 2.17 below.

Table 2.17: Patient category

Category	Definition
New	Never had treatment for TB infection in the past or who took treatment for <4 weeks
Previously treated	Treatment for TB infection in the past for ≥4 weeks and either completed or stopped for any reason (e.g., due to adverse events, developed TB, lost to follow-up)

Treatment outcomes

The treatment outcome possibilities for patients on TPT are completed, lost to follow-up, stopped or died as described in Table 2.18 below.

Table 2.18: Treatment outcomes

Outcome	Definition
Treatment completed	Treatment taken and completed within the prescribed period.
Lost to follow-up	Treatment interrupted for 4 consecutive weeks or more (if on ≤ 4months) OR two consecutive months (if on a course longer than 6 months) during the treatment period.
Treatment stopped	Treatment stopped during the treatment period, because of serious adverse events or development of TB disease.
Died	Death due to any cause during the treatment period

Stopping treatment

Treatment must be stopped if:

- Patient develops TB symptoms, collect sputum for TB NAAT testing or investigate by other means.
- If TB Positive start TB Treatment.
- Patient develops symptoms of hepato-toxicity, refer the patient to hospital immediately.
- Patient develops severe rash, refer patient to hospital urgently.
- Patient develops mild, continue treatment, add treatment for rash and monitor.

3. CLINICAL PRESENTATION OF PULMONARY AND EXTRA-PULMONARY

Module overview:

The module introduces signs and symptoms of TB including definition of Pulmonary and Extra- Pulmonary TB. The module also covers the different types of Extra-Pulmonary TB.

Learning outcomes:

By the end of this session, participants should be able to:

- Explain the clinical presentation of TB.

3.1. Pulmonary TB

Disease involving the lung parenchyma (portion of the lung involved in gas exchange). A patient with both parenchymal lesions in the lungs (Pulmonary TB) and Extra-Pulmonary TB is classified as Pulmonary TB. Miliary or disseminated TB is classified as PTB. It results from widespread blood borne dissemination of TB bacilli in all the organs including the lung tissue.

3.1.1. Symptoms in adults

The four common symptoms of pulmonary tuberculosis in adults used to **screen**, are:

Persistent cough

Fever of two weeks or more

Drenching night sweat

Unexplained weight loss of more than 1.5kg in a month

Drenching night sweatOther symptoms that may be present are:

- Shortness of breath
- Chest pain
- Coughing up blood
- Fatigue
- Loss of appetite

Note: People with TB disease can present without symptoms.

3.1.2. Symptoms in children

The 4 common symptoms of pulmonary tuberculosis in children used to screen are:

- Persistent non-remitting cough
- Persistent fever of 7 days or more
- Documented weight loss/failure to thrive (check Road to Health Booklet)
- Fatigue (less playful/always tired)

Documented loss of weight or unsatisfactory weight gain

Fatigue or reduced playfulness

Fever every day for 7 days or more

A productive cough is often accompanied by systemic symptoms such as fever, night sweats or loss of weight, is the commonest presentation of pulmonary tuberculosis.

Every patient with a positive symptom screen must be investigated appropriately. Not all those with TB will have a cough; therefore, a high index of suspicion is required, particularly in people who are HIV positive who may only have one of the above symptoms. A history of contact with a person with PTB increases the likelihood of a TB diagnosis and symptoms such as weight loss need to be investigated.

3.1.3. Physical signs

Physical signs refer to abnormalities indicative of a disease detectable by a clinician on examination of the patient. They may not be apparent to the patient.

On physical examination the signs may be non-specific, making it difficult to distinguish TB from other pulmonary diseases. These may include fever (body temperature high >38°C), increased pulse rate, abnormal chest sounds (crackles, wheeze, etc.), dullness on percussion. Physical signs may not be helpful in confirming the diagnosis, but it is important to examine the patient carefully. Some of the common signs are:

- ***Fever***: the body temperature may be high or irregular (greater than 38.5 °C)
- ***Pulse***: the pulse rate may be raised because of fever
- ***Chest***: there may be no abnormal signs, crackles in the lung apices more pronounced on deep breathing; localised wheeze in local obstruction or pressure; dullness where there is effusion and in chronic disease there may be extensive fibrosis with the trachea pulled to one side

3.2. Extra-Pulmonary TB (EPTB)

Extra-pulmonary TB can present with non-specific symptoms such as unintentional weight loss (more than 1.5 kg in a month), night sweats and fever for more than 2 weeks. Other symptoms depend on the site or organ affected. The most common types of extra-pulmonary tuberculosis are:

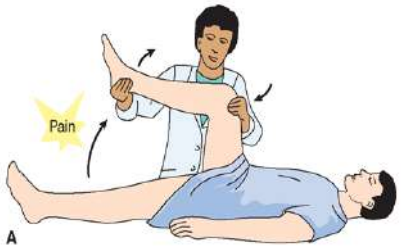
- TB lymphadenitis
- Tuberculosis pleural effusion (usually single-sided)
- TB of the bones and joints
- Tuberculosis pericardial effusion
- TB meningitis
- Disseminated/miliary tuberculosis
- TB peritoneal effusion

3.2.1. TB Meningitis

Tuberculous Meningitis (TBM) is a form of meningitis characterised by inflammation of the membranes (meninges) around the brain or spinal cord and caused by Mycobacterium tuberculosis.

Patients present with gradual onset of headache, accompanied by malaise, confusion, decreased consciousness, and sometimes vomiting.

One of the physically demonstrable symptoms of meningitis is **Kernig's sign**. Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees.

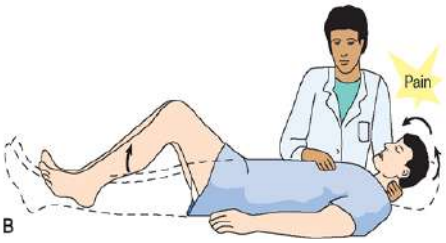


Examination to check Kernig's sign

Patient lies in supine position.

Flex one of the patient's legs at hip, and knee with the patient lying on back, and then slowly extend the leg at the knee/straighten the knee. Positive test elicited when:

- there is resistance to knee extension or
- pain in the lower back, from stretching of the meninges.



Another physically demonstrable symptom of meningitis is **Brudzinski's sign**. Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed.

Examination to check Brudzinski's neck sign

Patient lies in supine examination.

Flex the patient's neck forward slowly, towards the chest. Neck stiffness and involuntary bending of the knees and hips can indicate meningitis.

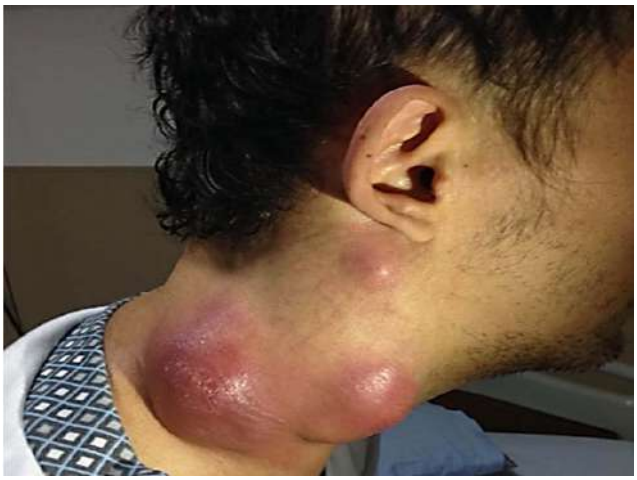
Patients presenting with severe neurological impairment (drowsiness, coma) have a greater risk of neurological complications after treatment.

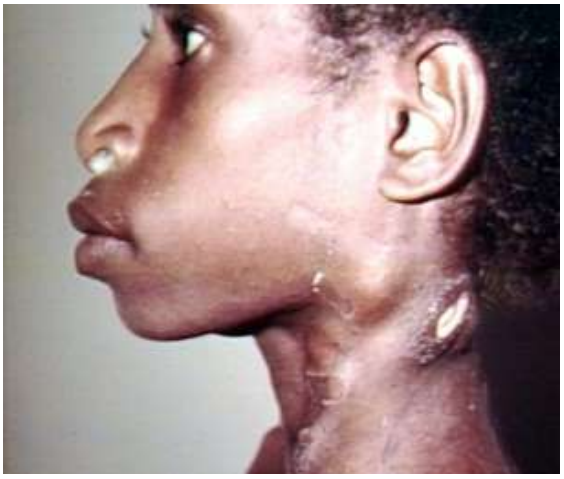
The patient must be referred to hospital as soon as TB meningitis is suspected.

Meningitis is the deadliest form of TB, particularly in persons co-infected with HIV. Early diagnosis and treatment can dramatically reduce the high mortality associated with this disease.

3.2.2. TB Lymphadenitis

TB lymphadenitis is among the most frequent presentations of extra-pulmonary TB. It involves enlargement of peripheral TB lymph nodes.

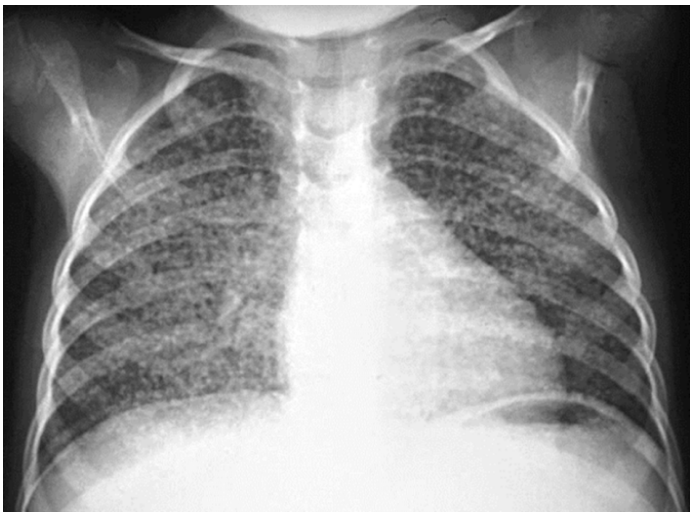




Cervical lymph node involvement is the most common. Commonly seen in children and young adults Lymph nodes are firm to fluctuant, fixed, asymmetrical, discrete or matted, non-tender, and may form an abscess or sinus/ fistula.

3.2.2. Disseminated/ Miliary TB

Miliary TB is a potentially life-threatening type of TB that occurs when a large number of the bacteria travel through the bloodstream and spread throughout the body.



Miliary TB is seen more commonly in infants, children less than 4 years old, and in immunocompromised people. Symptoms of miliary tuberculosis can be vague and the patient presenting with general deterioration in health. Disseminated TB usually develops insidiously with systemic symptoms such as fever, weakness, weight loss, fatigue, and anorexia or with symptoms attributable to involvement of one or more organ systems. Cough and dyspnoea also may be prominent symptoms. The chest radiograph typically shows the classic “miliary” pattern of diffuse small nodules.

3.2.4. TB Pleural Effusion

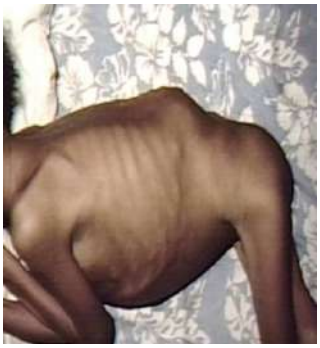
Tuberculous (TB) pleural effusion is a build-up of fluid in the space between the lining of the lung and the lung tissue (pleural space) after infection with tuberculosis. Presentation is often acute with non-productive cough, chest pain, shortness of breath and high temperature. The patient may have pleuritic pain (sharp, stabbing or burning pain in the chest when inhaling and exhaling, exacerbated by deep breathing, coughing, sneezing or laughing).

Chronic form is found in the elderly with symptoms of weakness, anorexia, weight loss, slight fever, cough and chest pain.

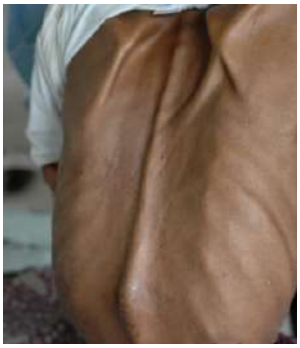
Clinical examination shows:

- Tracheal and mediastinal shift away from the side of the effusion
- Decreased chest movement
- Stony dullness on percussion on the side of the effusion

3.2.5. TB of Bones and Joints



TB of the bones most commonly affects the vertebral column. Children and adults can develop neurological symptoms and progressive paralysis. Back pain, stiffness and reluctance to bend the back or walk in children. There may be localised swelling, lump or abnormal curvature of the spine. In the early stages the physical examination can be non-specific. Patients with weakness or paraplegia should be referred to a specialist urgently.



3.2.6. Management of patients with EPTB

- Proper history taking, observation and physical assessment must be conducted to identify the site of disease.
- HIV testing must be offered to all patients with a previous negative or unknown HIV status.
- Emergency care must be provided for very sick patients at PHC level prior to referral to hospital.

Treatment for EPTB is the same as for PTB; Regimen 1 for 6 months (adults) and Regimen 3A or 3B for 6 months (children). In some instances of severe or complicated disease (meningitis, TB bones/joints, miliary TB) treatment may need to be extended to nine months. The intensive phase remains 2 months and the continuation phase is prolonged to seven months. – 2(RHZE)/7(RH).

Adherence counselling must be provided to patients. Response to treatment and treatment adherence must be monitored during follow up visits. Patients who missed appointments must be traced within 48 hours.

4. DIAGNOSIS OF TB

Module Overview:
The module introduces testing for TB. All testing activities should be accompanied by appropriate follow- up medical evaluation and treatment.

Learning Outcomes:
At the end of this module participants will be able to:

- Explain the role of specimens in the diagnosis of TB.
- Define priority groups for TB testing.
- Explain the process for specimen collection and referral of specimens to the laboratory.
- Explain the role of the laboratory in TB diagnosis.

Session outline
Duration: 60 minutes

Topics	Methods
Priority groups for testing	Interactive lecture and group discussion
Role of specimen in TB diagnosis	Interactive lecture and group discussion
Process for specimen collection and referral to the laboratory	Interactive lecture and group discussion Role play

4.1. Priority groups for TB testing

The Standard Operating Procedure (SOP) for screening and testing advocates for TB testing of the following groups:

- All people presenting with abnormal chest x-ray findings suggestive of TB irrespective of symptoms (DCXR Screening not included here as there is a separate document)
- All people presenting with any one TB symptom through

a) Self-screening
b) Screening conducted by HCW/ CHW (community)

SOP further promotes routine Targeted Universal Testing for TB (TUTT) in high-risk group irrespective of TB symptoms. The high-risk groups include:

- People living with HIV.

Newly diagnosed with HIV.
Pregnant women newly enrolled in Antenatal care.
People in HIV care at least once a year – during VL monitoring follow up visits.

- Household contacts of people diagnosed with DS-TB/ DR-TB. Recent contact, within the last 3 months before the start of current treatment. Conducted once after an exposure.
- People previously treated for TB in the past year.

With a known outcome of treatment completion or cure, to detect TB early in case of relapse. Test once after first year post treatment, then followed by symptom/ CXR screening afterwards.

4.2. Specimen for testing

4.2.1. Role of specimen in TB diagnosis:

Laboratory detection of Mycobacterium TB is dependent on the **quality** of the specimen provided. If the specimen is contaminated by food particles or not collected following deep breathing, it may result in an unsuccessful test result. To enhance the recovery of the Mycobacterium TB and ensure good quality results, the following are very important: proper specimen collection and prompt transportation to the laboratory.

4.2.2. Types of specimens

Mycobacterium TB can be recovered from several specimens, such as sputum, gastric aspirate, lymph node aspirates, pleural effusions, biopsies, cerebrospinal fluid, blood etc. However, the specimen usually collected from those presenting with symptoms of PTB is sputum. Sputum is mucus or phlegm coughed up from the lower airways (trachea and bronchi) in the lungs.

4.2.3. Factors contributing to rejection and incorrect test results

Laboratory testing of a specimen is a waste of time and resources if the following criteria are not fulfilled:

- Missing or inadequate identification.
- Spilled specimen.
- Insufficient quantity.
- Specimen collected in an inadequate container.
- Contamination suspected.
- Inappropriate transportation or storage.

These specimens will be rejected, the patient must be recalled, and a second specimen collected.

Factors contributing to rejection and incorrect test results include:

Clinical errors:

- Empty sputum containers.
- Specimen jar not properly closed resulting in leakage in transit.
- Saliva instead of sputum.
- Inadequate sample.
- Sputum inappropriately stored.
- Incorrect labelling of the sample, and mix-up of specimens.

Laboratory errors:

- Test failure.
- Accidental contamination in the laboratory.

4.2.4. Specimen collection and transportation

Process for specimen collection and referral to the laboratory

- Sputum specimens must be collected in a private, well-ventilated area.
- Where possible collection must be observed, the necessary infection control precautions taken.

Patient instruction

- The patient must be informed about the sputum collection process.
- Rinse your mouth with water.
- Hold the container with a tissue.
- Open the container without touching the inside of the lid and container.
- Take two deep breaths and on the third time, cough deeply from your chest.
- Hold the sputum container close to your mouth.
- Spit into the container without contaminating the outside.
- Repeat steps 2 and 3 until at least 5ml (1 – 2 tablespoons) of specimen is obtained
- Screw the lid of container tightly.
- Wipe clean any spillage on the outside of the container.

Checking quality of sputum specimen

- Healthcare worker should put on gloves.
- Check if the container is tightly closed.
- Check if the specimen collected is correct and adequate

a) Consistency mucoid, may be clear, purulent or blood tinged

b) At least 5ml of specimen must be collected, if less the patient should be requested to produce more.

Quality of sputum specimen

Post Sputum collection procedure

- Label the specimen container with the patient's name, folder number, date and time of specimen collection.
- Peel-off one of the pre-printed barcoded labels from the laboratory request form and place horizontally on the specimen container.

Laboratory request form and specimen plastic bag

- Complete the laboratory request form. Ensure all information is completed, if there is any missing information in patient folder verify with patient.
- Place the specimen container and request form in the appropriate compartments of the specimen plastic bag.
- If more than one specimen is collected from a patient, all the specimens should be placed in one bag with the relevant request form/s.
- Inform the patient on estimated date of results and how these will be communicated.
- Provide a follow-up appointment date for TB results.

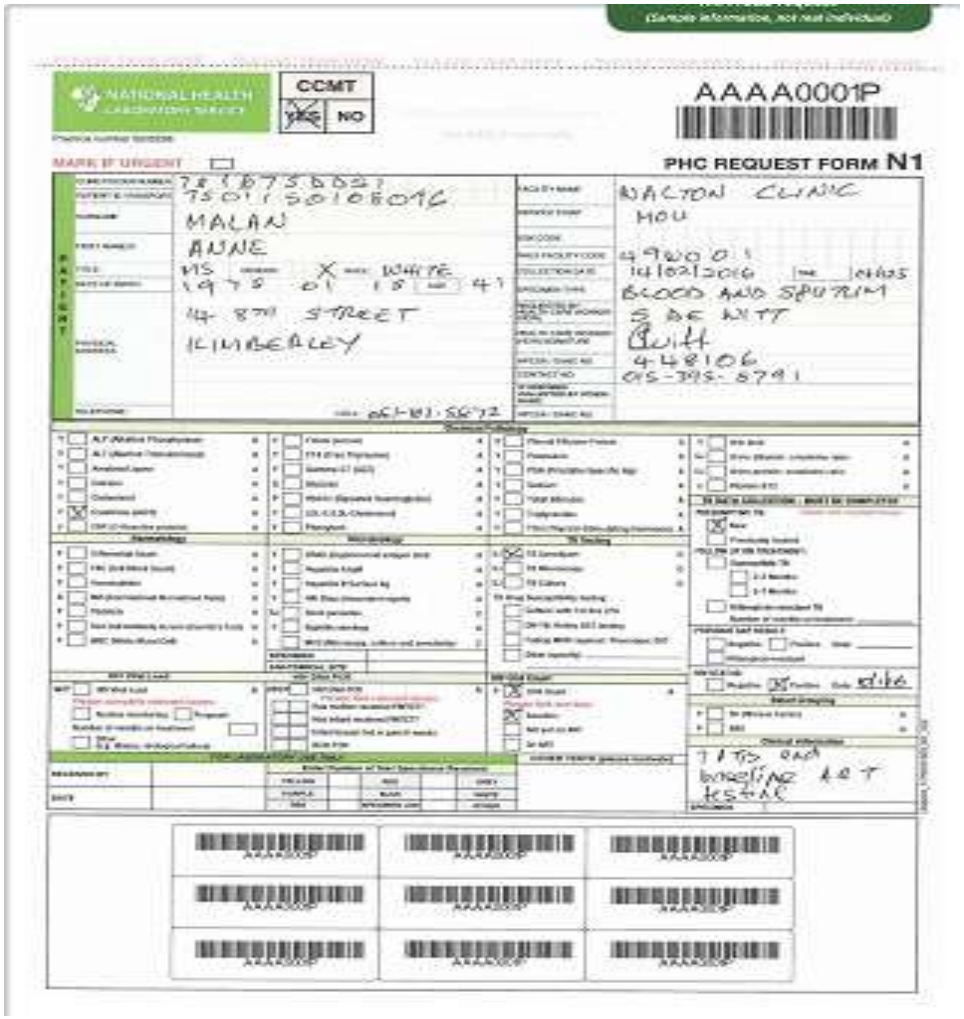


Figure4.1: Completion of a laboratory form

Indicate whether the investigation required is for a patient:

Presumed to have TB (symptomatic or not)

New
Previously treated

Follow up, i.e., patient who is already on treatment

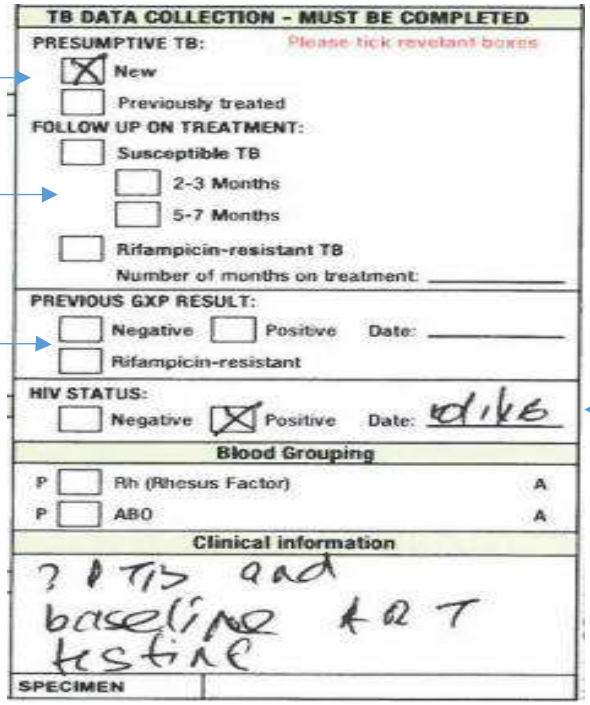
At conversion (2 months or 3 months)
End of treatment (5-7 months)
For RR-TB write number of months on treatment

Indicate result of previous TB NAAT test and date

If a repeat TB NAAT test is required (following an unsuccessful test), or

If a culture and DST is required following a negative TB NAAT in PLHIV, or

If a smear microscopy test is required following a positive TB NAAT result.


TB DATA COLLECTION - MUST BE COMPLETED
PRESUMPTIVE TB: Please tick relevant boxes
[X] New
[ ] Previously treated
FOLLOW UP ON TREATMENT:
[ ] Susceptible TB
[ ] 2-3 Months
[ ] 5-7 Months
[ ] Rifampicin-resistant TB
Number of months on treatment: _____
PREVIOUS GXP RESULT:
[ ] Negative [ ] Positive Date: _____
[ ] Rifampicin-resistant
HIV STATUS:
[ ] Negative [X] Positive Date: old
Blood Grouping
P [ ] Rh (Rhesus Factor) A
P [ ] ABO A
Clinical information
? PTB and baseline for RT testing
SPECIMEN

Tick HIV Status and data tested where it is known
Include relevant clinical information i.e. type of TB suspected and type of specimen collected

Figure 4.2: Continuation of laboratory form

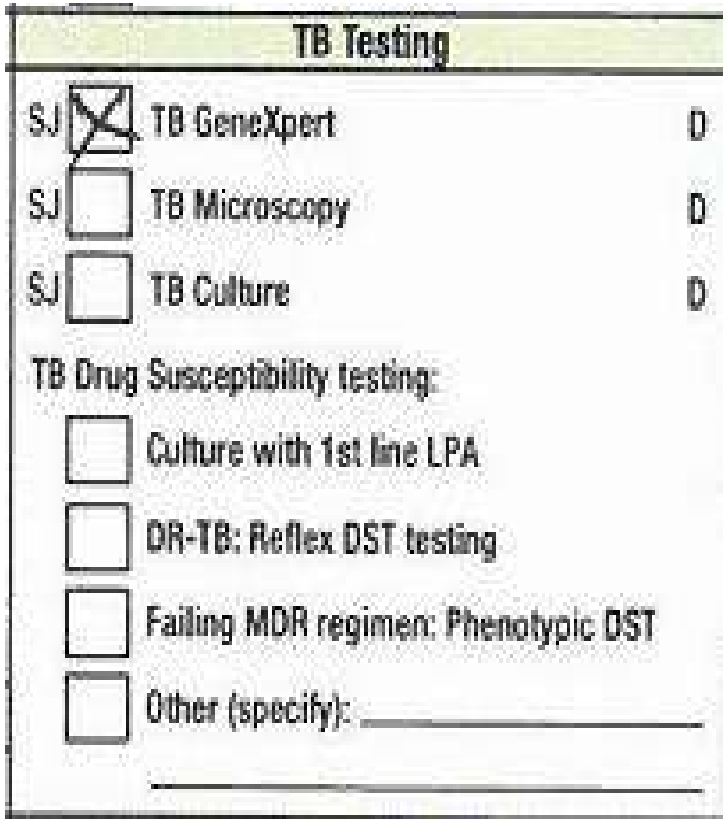
Tick the test required:

- GeneXpert MTB/RIF
- TB Smear Microscopy (for TB NAAT positive/MTB detected only)
- Culture

If first line DST is required tick

- TB Culture and
- TB Line Probe Assay (MTBDR)

For second line DST tick



Storage and transportation of the specimen

- Avoid exposure of specimens to direct sunlight.
- Specimens can be stored at room temperature (20-25ºC) up to 24 hours.
- Where room temperature is higher than 25º they should be stored in a fridge.
- Do not store in a freezer.
- Transportation of the specimen should be as soon as possible.
- During transportation specimens should be transported upright in a cooler box.

Table 4.1: Obtaining sputum specimen in patients who cannot expectorate

Method	Description	Advantage	Disadvantage
Nebulisation / sputum induction	Patients inhales a saline mist which causes them to cough.	Used to obtain sputum in patients with non-productive cough. Easy to perform.	Specimen may be watery and confused with saliva. Requires special equipment.
Gastric aspirate	A tube is inserted into the stomach through the patients nose to obtain swallowed sputum.	Used to obtain sputum in children who do not cough up sputum.	Must be done early in the morning before eating. Patients may need to be hospitalised. It is an uncomfortable procedure for the patient.
Bronchoscopy	A scope is passed through the mouth or nose to the disease part of the lung to obtain sputum or lung tissue.	Used to obtain sputum when the patient cannot cough and gastric. aspirate cannot be done.	Invasive procedure. Requires special equipment. Must be done in a hospital by a specialist. Requires anaesthesia.

Role play

Aim of the role play:

- Role play to practice educating patients on the importance of proper sputum collection
- To practice how to provide clear instructions to patients on the sputum collection procedure

5. TB DIAGNOSTIC TESTS

Module overview:
The module is about the diagnostic tests used in identifying patients with active TB disease. All testing activities should be accompanied by appropriate follow-up medical evaluation and treatment.

Learning outcomes:
At the end of this module participants will be able to:

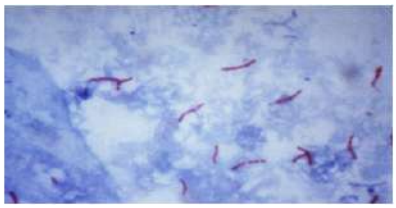
- Explain the role of each test in the diagnosis of TB.
- Describe steps involved in the diagnosis of TB based on the laboratory test results.
- Interpret laboratory test results.
- Describe the steps to follow on receiving laboratory results.

5.1. Smear Microscopy

Definition
Smear microscopy is a visualization of stained TB bacilli in clinical specimens, using microscope. Specimens for testing: sputum, gastric aspirate, or another clinical specimen.

Indication for smear microscopy
Smear microscopy is used as a baseline test for all patients who are TB NAAT positive and for follow up bacteriological monitoring.

Advantages and disadvantages of smear microscopy



Source: CDCPhil.gov

Strengths	Limitations
- Identifies the most infectious TB cases (i.e., sputum positive). - Relatively easy to perform. - Short TAT. - Essential for monitoring TB treatment response.	- Low sensitivity (Sensitivity in high HIV prevalence settings can drop to as low as 20%). - Cannot differentiate between drug-sensitive and drug-resistant TB. - Variable performance that depends on the experience of the technologist.

5.2. TB Culture

Definition

TB culture is the gold standard in TB diagnosis. It involves growing the Mycobacteria in the laboratory from the specimen, either on solid or liquid media.

Indications

- To diagnose paucibacillary disease in presumptive TB cases who have a negative TB NAAT result (MTB not detected), despite clinical signs and symptoms suggestive of TB. i.e Children, PLHIV, and in people with extra-pulmonary TB
- Where drug susceptibility testing (DST) is required.
- Where confirmation of live bacteria is required.
- Patients who remain smear-positive at the end of the intensive/ continuation phase of treatment or who do not improve clinically during treatment.

Table 5.1: Strengths and weaknesses of TB culture

Strength	Limitations
• High sensitivity, detects a higher proportion of cases among patients with symptoms.	• Slow diagnostic technique with a long TAT (14 days or more). • High contamination rate.

5.3. Drug Susceptibility Testing (DST) Definition

Drug susceptible testing (DST) is the testing for sensitivity of MTB isolates to several medicines used for the treatment of TB. First line DST conducted for Rifampicin and Isoniazid mainly but also available for Ethambutol, Pyrazinamide on request. Second line DST conducted for aminoglycosides, fluoroquinolones.

5.4. TB NUCLEIC ACID AMPLIICATION TESTS (TB NAATs)

Definition

TB Nucleic Acid Amplification Tests (TB NAATs) are rapid molecular tests in which bacterial genetic material (i.e. TB DNA) is amplified (copied) in a process known as polymerase chain reaction (PCR). The amplification step is necessary because in many cases the amount of DNA in a sample is very small. The amplification of TB DNA therefore enables the TB NAAT tests to detect Mycobacterium tuberculosis material, even if only very small amounts are present in the tested sample. In addition to detecting Mycobacterium tuberculosis, they also detect the resistance of TB strains to certain TB drugs used to treat the disease.Three TB NAAT assays that have been approved by the National TB Programme as first-line (front- line) tests for the investigation of TB in clinical specimens. They are:

- Xpert MTB/RIF Ultra,
- BD MAX MDR-TB and
- cobas MTB and cobas MTB-RIF/INH assays.

All three assays are automated TB testing platforms.

- Automated means that most of the steps involved in the processing of clinical specimens with these assays occur within the instruments, with minimal or no human intervention.
- Only the sample treatment step, where the sample is treated with the sample treatment reagent, occurs manually.
- The rest of the steps which include DNA extraction, DNA amplification, detection and results interpretation, are automated.

Results are typically available in 24 to 48 hours. This allows for:

- early diagnosis of TB,
- early initiation of appropriate treatment,
- reduced period of infectiousness, and
- improved patient outcomes.

Indication

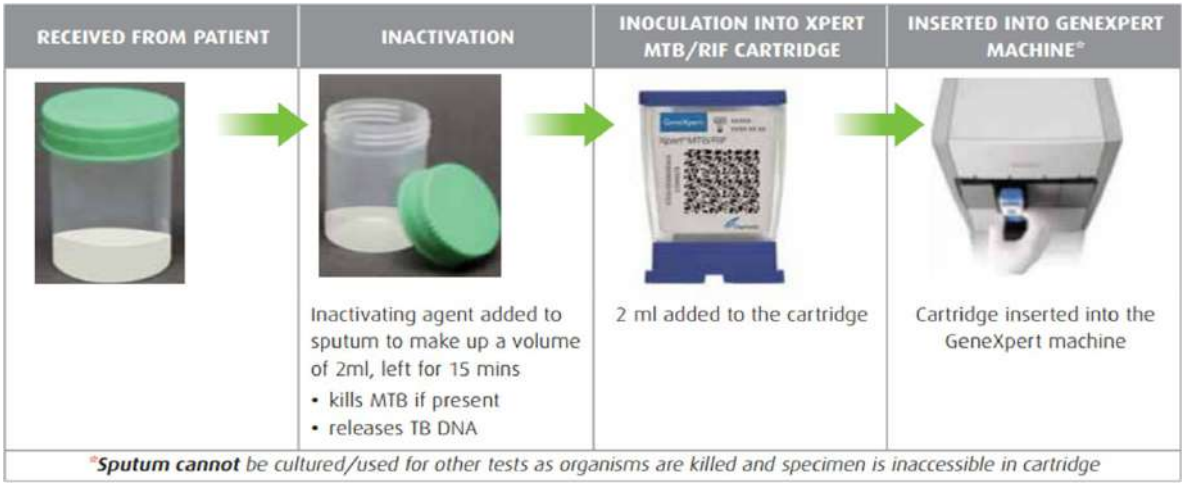
- TB NAAT is the frontline test that we use in the diagnosis of TB in South Africa
- Used in the primary diagnosis of TB in people eligible for TB testing (with/out symptoms)

5.4.1 Xpert® MTB/RIF Ultra

It is a fully automated molecular assay (i.e., PCR test) that is used to detect Mycobacterium tuberculosis and Rifampicin resistance from the same specimen at the same time in < 2 hours.

The test involves three manual steps:

- addition of reagent to liquefy and inactivate specimen
- transfer of 2ml of liquefied specimen into the cartridge
- loading of the cartridge onto the instrument



Indication

- It is currently one of the TB NAAT assays that have been approved by the NTP as frontline tests for investigation of TB in clinical specimens.
- Used in the initial diagnosis of TB in people eligible for TB testing (with/out symptoms)
- It can be used on the following specimens other than sputum:
  - Any specimen type of respiratory origin, including gastric washings/aspirates
  - Lymph node biopsies or fine needle aspirates
  - Tissue biopsies
  - Fluids (joint, pleural, ascitic, peritoneal, pus collection)
  - Cerebrospinal fluid (CSF)

Strengths and Weaknesses

Strengths	Weaknesses
• It is specific for the MTB complex • Short Turnaround Time (TAT) • Detects MTB and RIF Resistance (High sensitivity for RIF Resistance)	• ·Reduced sensitivity in smear negative cases • ·Does not detect INH resistance • It cannot be used for monitoring response to treatment

5.4.2 BD MAX MDR-TB Assay

The BD MAX™ MDR-TB assay is a PCR-based molecular diagnostic test that can simultaneously detect the bacteria that cause tuberculosis (TB) and determine whether the bacterial strain detected is sensitive or resistant to two important first-line drugs, rifampicin and isoniazid (INH), in a single test.
This is important as it helps to decide which treatment regimen should be used in patients diagnosed with TB. The system is fully automated, which reduces the possibility of human error and increases the speed to result.
The test is validated for use with sputum samples only. Up to 24 samples can be tested simultaneously per run on the computerised benchtop system, with results automatically released within four (4) hours.

5.4.3 Cobas MTB and Cobas MTB/RIF/INH

The NHLS has acquired two TB-NAATs from Roche Molecular Systems, the cobas MTB and the cobas MTB-RIF/INH assay. Cobas MTB detects the presence of MTB in clinical samples.
The cobas MTB-RIF/INH assay detects resistance to rifampicin or isoniazid. Samples that are positive with cobas MTB are then tested for resistance to rifampicin and isoniazid with cobas MTB-RIF/INH.
These tests have been validated for use with sputum samples only. Each of these assays can provide results for 96 tests (including assay controls).

5.5 Who must be tested for TB?

A specimen must be collected for TB testing in the following groups:

- People (children, adolescents, and adults) with any one of the TB symptoms.
- People who have been in close contact with a person diagnosed with TB in the past year irrespective of TB symptoms.
- People who have been treated and completed TB treatment in the past two years irrespective of TB symptoms.
- Newly diagnosed PLHIV irrespective of symptoms.

Frequency of testing

1. General population
   - Only when they present with any TB symptom or digital chest x-ray changes suggestive of TB.
2. People living with HIV.
   - At the time of HIV diagnosis
   - On enrolment in Antenatal care for pregnant women
   - Annually for PLHIV on treatment linked to VL monitoring follow up visits.
3. Household contacts of people diagnosed with TB.
   - Recent contact, within the last the 3 months before the start of current treatment
   - After each exposure to a person with a confirmed TB diagnosis
4. People previously treated for TB.
   - Annually for a period of two years

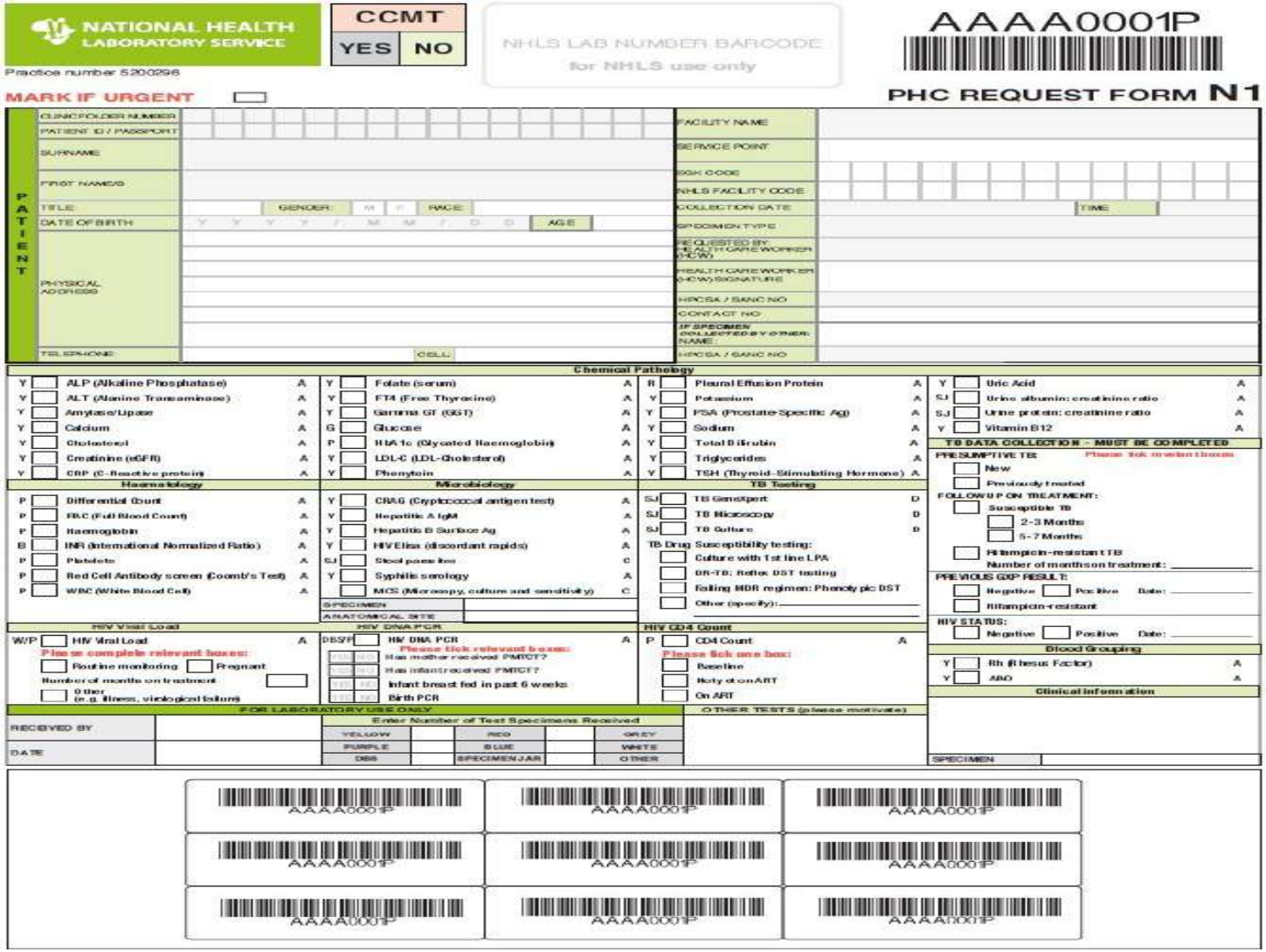
In-between the annual testing, PLHIV and people previously treated for TB must be screened for TB symptoms and tested only if symptomatic.

5.6 Process of investigating TB in clinical specimens

In South Africa, the TB-NAAT tests (i.e. Xpert MTB/RIF Ultra, BD MAX MDR-TB, cobas MTB and cobas MTB-RIF-INH assays) are first-line (front-line) tests that should be used when testing for TB in clinical samples. Clinicians must do the following:

- Record the patient in the TB identification register
- Collect one spot specimen for the TB-NAAT under supervision
- Label the specimen container correctly
- Complete the laboratory form and provide all required information
- Send the specimen promptly to the laboratory, preferably in a cooler box and protected from sunlight.

Laboratory form



NATIONAL HEALTH LABORATORY SERVICE

Practice number 5200296

CCMT — YES / NO

NHLS LAB NUMBER BARCODE for NHLS use only

AAAA0001P

PHC REQUEST FORM N1

MARK IF URGENT

PATIENT

CLINIC FOLDER NUMBER
PATIENT ID / PASSPORT
SURNAME
FIRST NAMES
TITLE | GENDER: M F | RACE
DATE OF BIRTH: Y Y Y Y / M M / D D | AGE
PHYSICAL ADDRESS
TELEPHONE | CELL

FACILITY NAME
SERVICE POINT
BOSK CODE
NHLS FACILITY CODE
COLLECTION DATE | TIME
SPECIMEN TYPE
REQUESTED BY: HEALTH CARE WORKER (HCW)
HEALTH CARE WORKER (HCW) SIGNATURE
HPCSA / SANC NO
CONTACT NO
IF SPECIMEN COLLECTED BY OTHER: NAME
HPCSA / SANC NO

Chemical Pathology

Y		ALP (Alkaline Phosphatase)	A	Y		Folate (serum)	A	R		Pleural Effusion Protein	A
Y		ALT (Alanine Transaminase)	A	Y		FT4 (Free Thyroxine)	A	Y		Potassium	A
Y		Amylase/Lipase	A	Y		Gamma GT (GGT)	A	Y		PSA (Prostate-Specific Ag)	A
Y		Calcium	A	G		Glucose	A	Y		Sodium	A
Y		Cholesterol	A	P		HbA1c (Glycated Haemoglobin)	A	Y		Total Bilirubin	A
Y		Creatinine (eGFR)	A	Y		LDL-C (LDL-Cholesterol)	A	Y		Triglycerides	A
Y		CRP (C-Reactive protein)	A	Y		Phenytoin	A	Y		TSH (Thyroid-Stimulating Hormone)	A

Y		Uric Acid	A
SJ		Urine albumin: creatinine ratio	A
SJ		Urine protein: creatinine ratio	A
Y		Vitamin B12	A

Haematology

P		Differential Count	A
P		FBC (Full Blood Count)	A
P		Haemoglobin	A
B		INR (International Normalized Ratio)	A
P		Platelets	A
P		Red Cell Antibody screen (Coomb's Test)	A
P		WBC (White Blood Cell)	A

Microbiology

Y		CRAG (Cryptococcal antigen test)	A
Y		Hepatitis A IgM	A
Y		Hepatitis B Surface Ag	A
Y		HIV Elisa (discordant rapids)	A
SJ		Stool parasites	C
Y		Syphilis serology	A
		MCS (Microscopy, culture and sensitivity)	C

SPECIMEN
ANATOMICAL SITE

TB Testing

SJ		TB GeneXpert	D
SJ		TB Microscopy	D
SJ		TB Culture	D

TB Drug Susceptibility testing:
- Culture with 1st line LPA
- DR-TB: Reflex DST testing
- Failing MDR regimen: Phenotypic DST
- Other (specify): _____

TB DATA COLLECTION - MUST BE COMPLETED

PRESUMPTIVE TB: Please tick relevant boxes
- New
- Previously treated

FOLLOW UP ON TREATMENT:
- Susceptible TB
  - 2-3 Months
  - 5-7 Months
- Rifampicin-resistant TB

Number of months on treatment: _____

PREVIOUS GXP RESULT:
- Negative / Positive — Date: _____
- Rifampicin-resistant

HIV STATUS:
- Negative / Positive — Date: _____

HIV Viral Load

W/P | | HIV Viral Load | A

Please complete relevant boxes:
- Routine monitoring
- Pregnant

Number of months on treatment: _____
- Other (e.g. Illness, virological failure)

HIV DNA PCR

DBS/P | | HIV DNA PCR | A

Please tick relevant boxes:
- Has mother received PMTCT?
- Has infant received PMTCT?
- Infant breast fed in past 6 weeks
- Birth PCR

HIV CD4 Count

P | | CD4 Count | A

Please tick one box:
- Baseline
- Roty ot on ART
- On ART

Blood Grouping

Y		Rh (Rhesus Factor)	A
Y		ABO	A

Clinical information

FOR LABORATORY USE ONLY

RECEIVED BY
DATE

Enter Number of Test Specimens Received

YELLOW		RED		GREY	
PURPLE		BLUE		WHITE	
DBS		SPECIMEN JAR		OTHER	

OTHER TESTS (please motivate)

SPECIMEN

AAAA0001P (x9)

Role of the laboratory

- The laboratory will test the specimen, and
- Communicate results back to the facility
- Inform patients of their results - SMS notification
- This should be within 48 hours

5.7 Interpretation of results and action to be taken

5.7.1 Possible TB NAAT results

There are seven (7) possible TB NAAT results, and they are reported as follows:

Results	TB NAAT ASSAY		
	Xpert MTB/RIF	BD MAX MDR-TB	Cobas MTB & Cobas MTB-RIF/INH
MTB Detected, Rifampicin Unsuccessful	Yes	Yes	Yes
MTB Detected, Rifampicin Susceptible	Yes	Yes	Yes
MTB Detected, Rifampicin Susceptible & Isoniazid Resistant	No	Yes	Yes
MTB Detected, Rifampicin resistant	Yes	Yes	Yes
MTB Detected, Rifampicin Resistant & Isoniazid Resistant	No	Yes	Yes
Trace	Yes	Yes	Yes
MTB Not Detected	Yes	Yes	Yes

Results meaning and follow-up action

1. **Results of test determine presence of absence of Mycobacterium tuberculosis (MTB)**

Result	Meaning	Action by the clinician
MTB complex detected	• MTB was isolated from the specimen • The patient has bacteriologically confirmed TB and should be treated.	• The clinician should initiate the patient on appropriate TB treatment • Appropriate treatment will be guided by rifampicin and isoniazid resistant status
MTB complex not detected	• MTB was not isolated from the specimen. • It means that TB disease could not be confirmed bacteriologically	• Further investigations are required to confirm TB. • The clinician should request another specimen, for culture

	• This does not exclude TB in people with paucibacillary disease, i.e. children, HIV positive and those with extrapulmonary TB	and drug susceptibility testing (DST)

2. Results of test to determine susceptibility or resistance to rifampicin (RIF) only (Xpert MTB/RIF Ultra), rifampicin (RIF) and Isoniazid (INH) (BD Max MDR-TB and Cobas MTB-RIF/INH)

Result	Meaning	Action by the clinician
Rifampicin unsuccessful	• Rifampicin testing was unsuccessful for the TB strain detected.	• Submit another specimen for smear microscopy, culture and DST • Start the patient on 1st line TB treatment and monitor response to treatment • Review culture and DST results when they become available
Rifampicin sensitive	• The MTB strain isolated is sensitive to rifampicin • For patients tested with GXP, this does not exclude the possibility of the isolated strain being resistant to other 1st line drugs, Isoniazid, pyrazinamide and ethambutol. • For patients tested with BD MAX, this means the strain isolated is also sensitive to isoniazid. However this is not reported in the results. However this result does not exclude the possibility of resistance to pyrazinamide and ethambutol.	• Submit another sample for baseline smear microscopy • Start the patient on first line treatment
Rifampicin sensitive & Isoniazid resistant	• The strain isolated from the patient specimen is sensitive to rifampicin but resistant to isoniazid, • This means isoniazid - resistant TB has been detected.	• Submit another specimen for DR-TB reflex testing • Start the patient on isoniazid - resistant TB treatment • Follow-up DR-TB reflex testing results for fluoroquinolone status

Rifampicin resistant	• The MTB strain isolated was resistant to rifampicin • For patients tested with GXP, this does not exclude to possibility of resistance to other 1st line drugs, Isoniazid, pyrazinamide and ethambutol. • For patients tested with BD MAX, this means the strain isolated is sensitive to isoniazid, however this does not exclude the possibility of the strain being resistant to pyrazinamide and ethambutol • The patient has rifampicin - resistant TB (RR-TB)	• If the health facility is a DR- TB treatment initiation site, submit a specimen for DR - TB reflex testing and initiate appropriate treatment as per DR-TB guidelines. • If the health facility is NOT a DR-TB treatment initiation site, refer the patient to the DR -TB treatment initiation site for further management.
Rifampicin resistant & Isoniazid resistant	• The strain isolated from the patient's specimen is resistant to both rifampicin and isoniazid, the two potent 1st line TB drugs. • An MDR-TB strain has been detected in the patient's specimen	• If the health facility is a DR- TB treatment initiation site, submit a specimen for DR - TB reflex testing and initiate appropriate treatment as per DR-TB guidelines. • If the health facility is NOT a DR-TB treatment initiation site, refer the patient to the DR -TB treatment initiation site for further management

3. Trace and test unsuccessful

Result	Meaning	Action by the clinician
Trace	• A very low amount of MTB DNA was detected in the specimen • When a low amount of MTB DNA is detected, the status regarding rifampicin and isoniazid will be reported as rifampicin unsuccessful by TB NAAT assays.	• Manage the patient as per the TRACE diagnostic algorithm
Test unsuccessful	• The test was unsuccessful. • This may be due to poor quality specimen of technical causes	• A new specimen must be collected for a repeat TB NAAT testing

5.7.2 Factoring in previous TB treatment period

This increased sensitivity of TB-NAAT tests can lead to the detection of residual genetic material from dead bacilli in patients who have previously been treated for TB.

Therefore, in individuals who have completed TB treatment in the last two years, a “positive" or “trace" result may indicate the presence of either live bacilli (active TB disease) or dead bacilli (remnants of a previous TB episode).

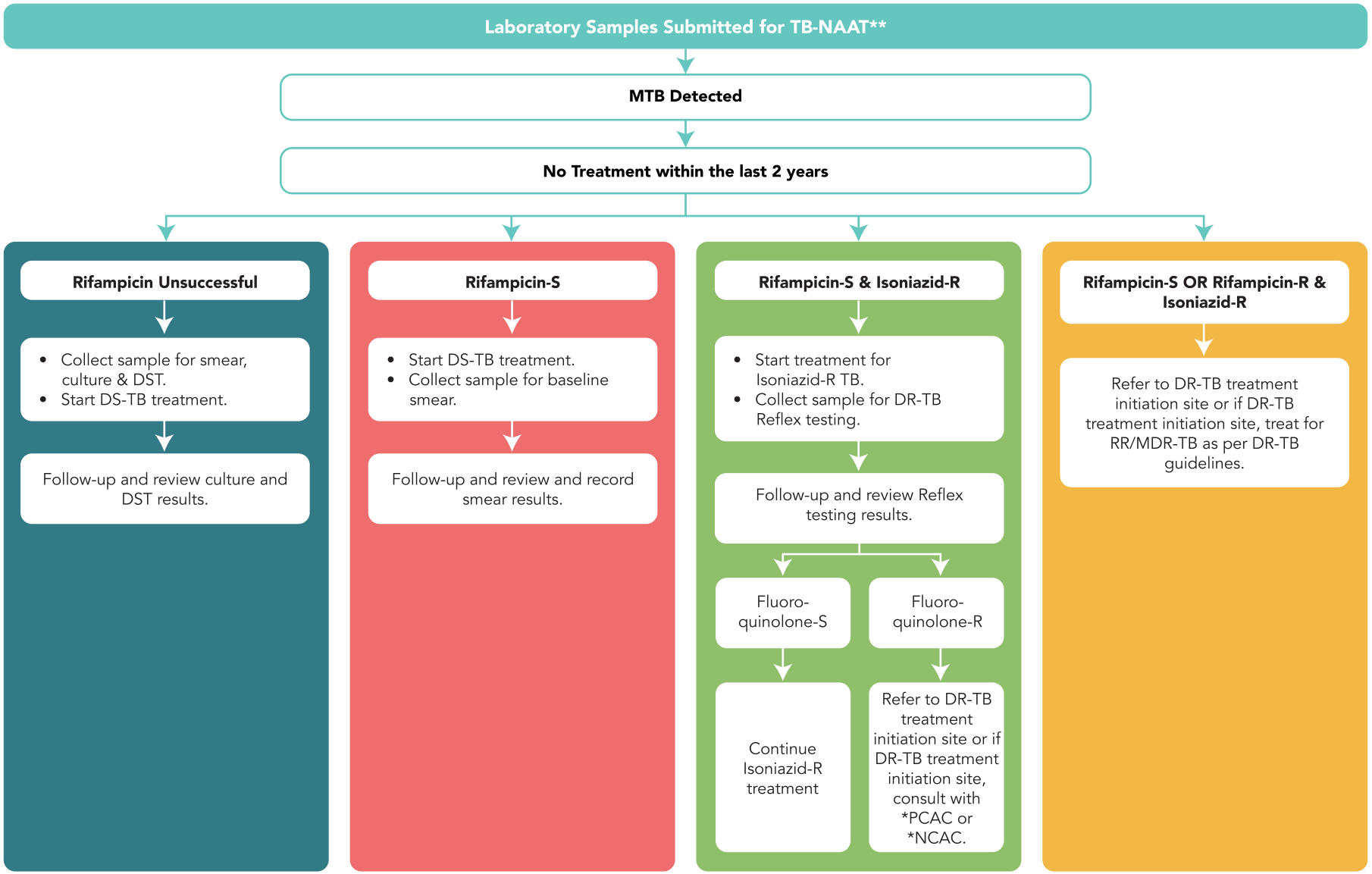
The test results must therefore be considered along with the clinical findings before starting treatment and a TB culture performed to confirm active TB disease.

MTB detected results

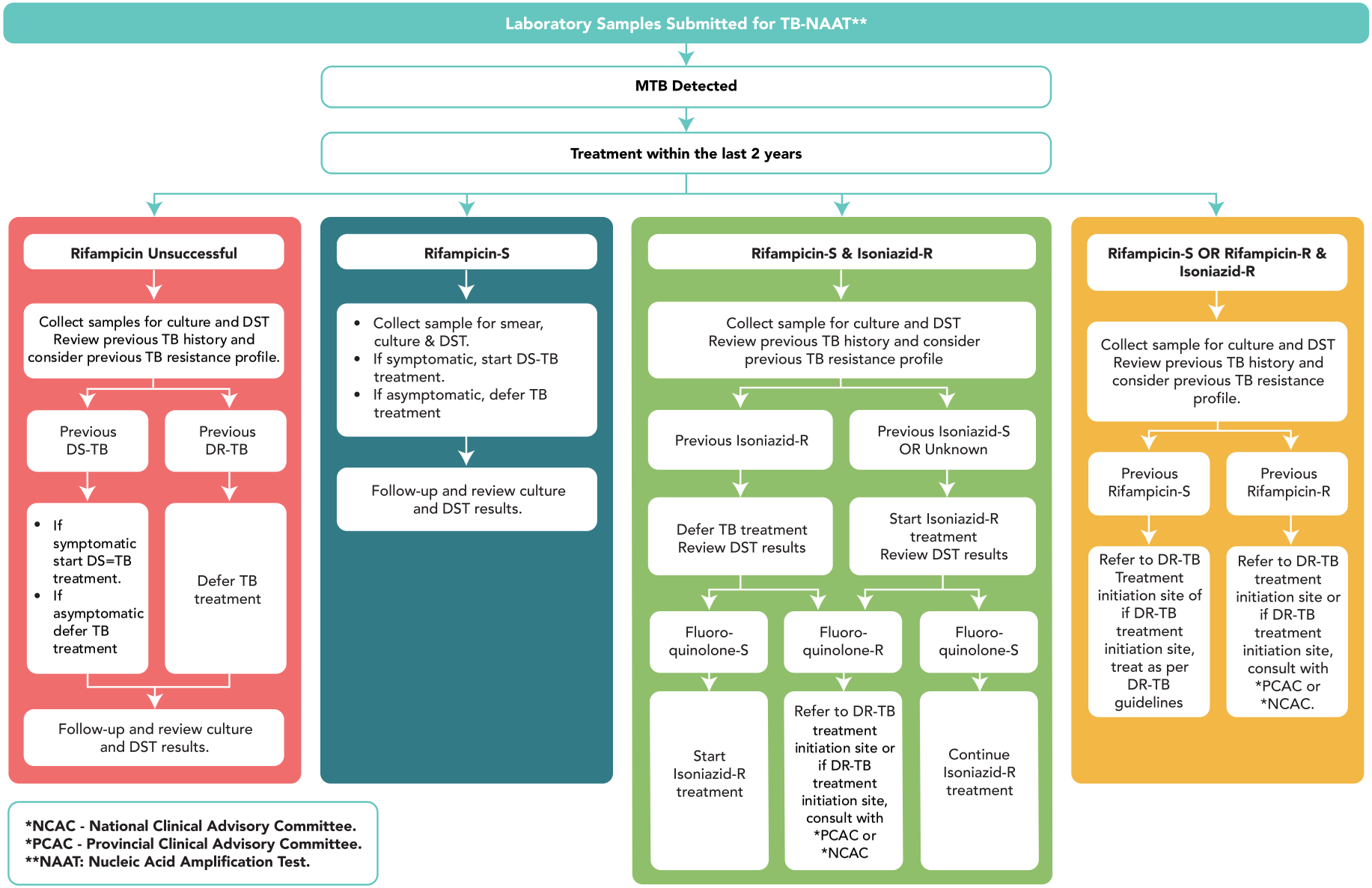
The result “MTB detected” in sputum must be confirmed by culture and DST. This is to avoid unnecessary treatment of these patients. The threshold for previously treated patients is two years. This therefore does not apply to patients who were treated more than 2 years ago

Trace results

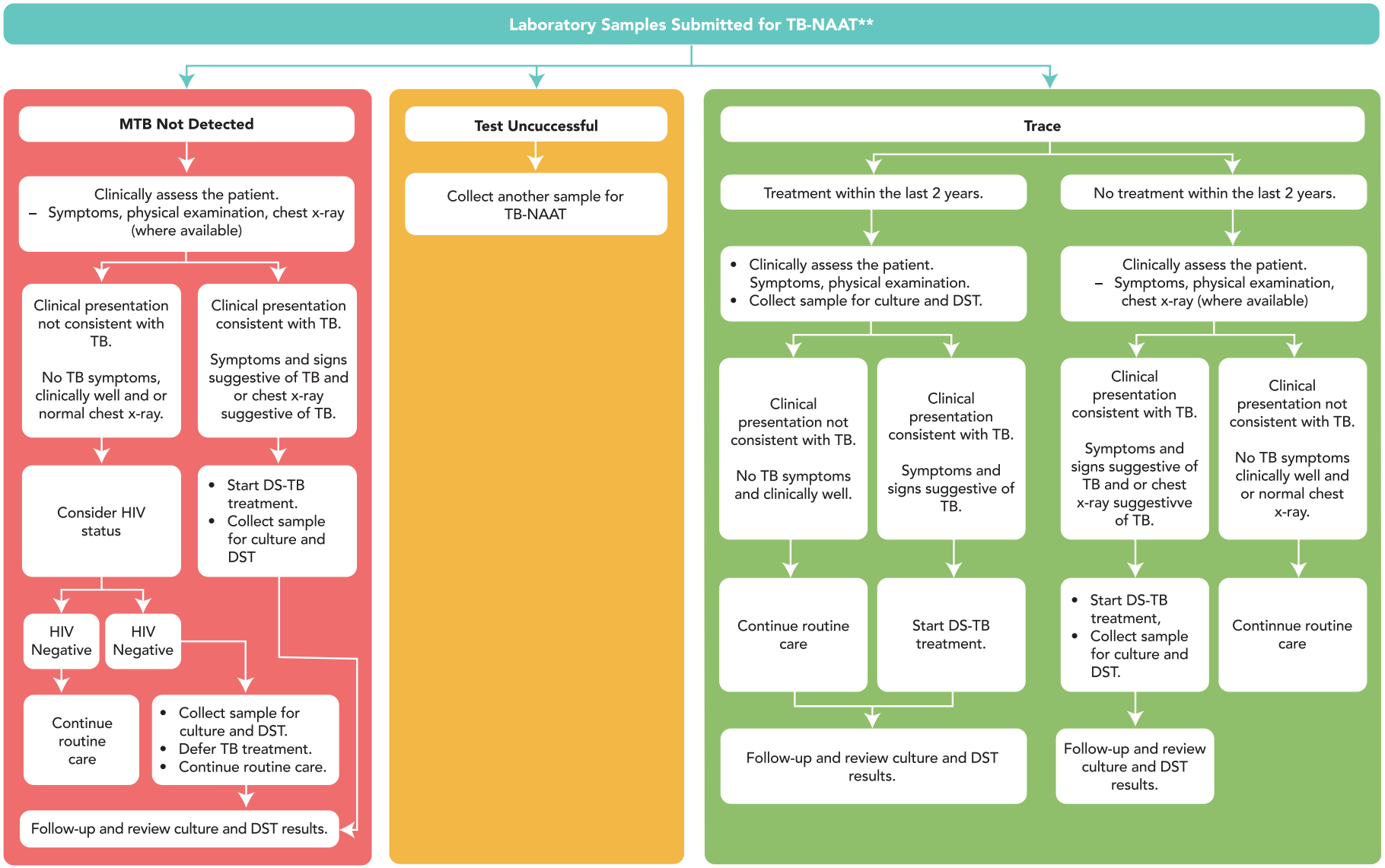
For “trace" results where a patient has received TB treatment within the last two years, this result must be confirmed by culture and DST. An exception to this is EPTB samples, where a “trace" result should be treated as “MTB Detected, Rifampicin unsuccessful”.



***NCAC - National Clinical Advisory Committee.**
***PCAC - Provincial Clinical Advisory Committee.**
****NAAT: Nucleic Acid Amplification Test.**



***NCAC - National Clinical Advisory Committee.**
***PCAC - Provincial Clinical Advisory Committee.**
****NAAT: Nucleic Acid Amplification Test.**



***NCAC - National Clinical Advisory Committee.**
***PCAC - Provincial Clinical Advisory Committee.**
****NAAT: Nucleic Acid Amplification Test.**

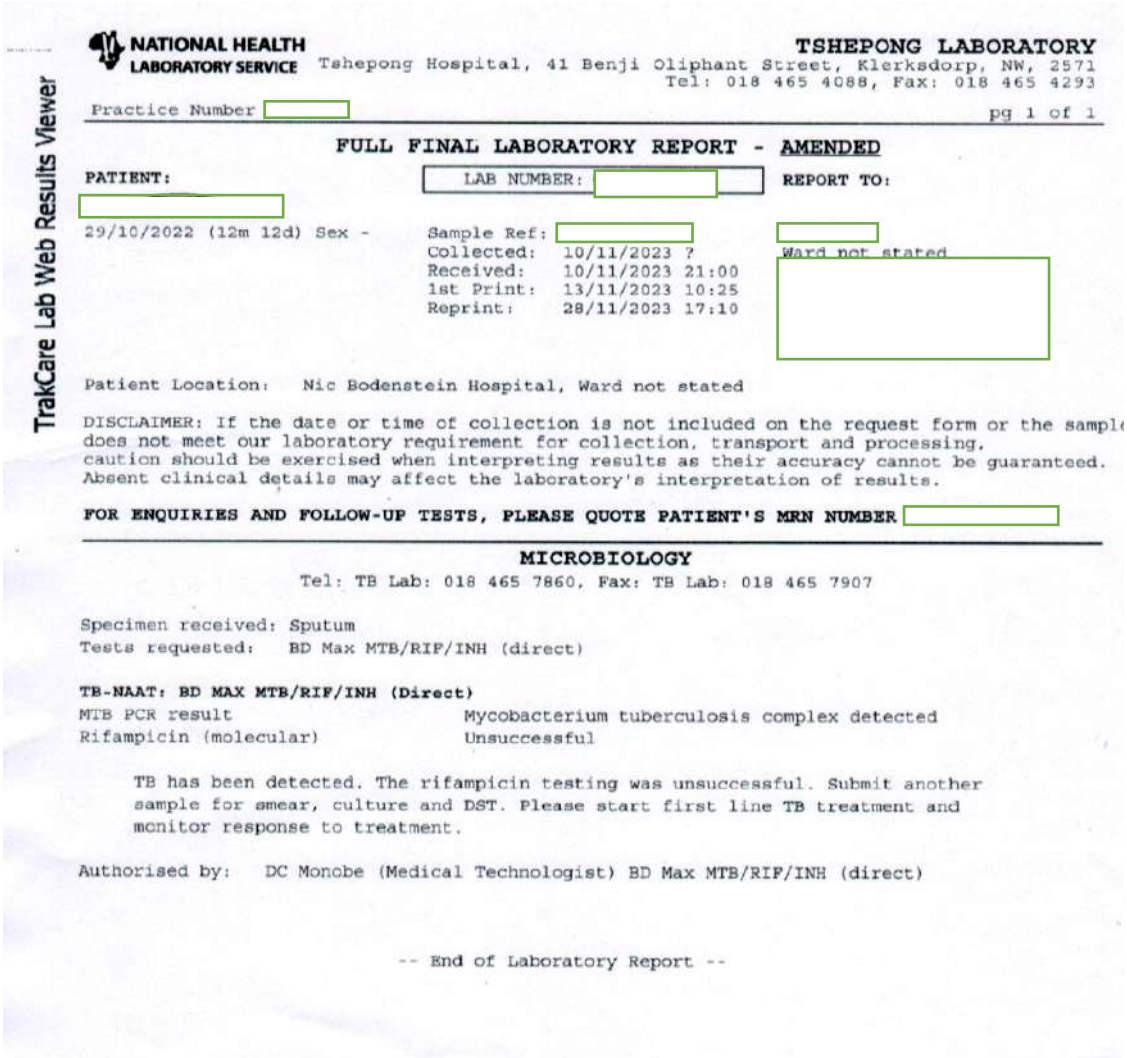
5.7.3 Follow-up of patient after receiving laboratory results

Patient must be given a return date within 2 days for results and initiation of treatment. If results confirm DS-TB:

- Inform the patient of the result
- Educate and inform the patient about the TB disease
- Take a medical history and assess the patient clinically
- Obtain sputum for smear microscopy (pre-treatment) for monitoring.
- Patient does not need to return for pre-treatment smear microscopy results.
- Initiate TB treatment
- Inform the patient about the treatment and provide adherence counselling
- Complete the patient clinical record and keep laboratory results in same folder
- Inform the patient about the importance of screening of contacts and obtain information about close contacts
- Arrange for screening of close contacts
- Give patient appointment for next follow up visit

Follow-up patients who do not return on specified date

5.7.4 Samples of laboratory results



TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

TSHEPONG LABORATORY
Tshepong Hospital, 41 Benji Oliphant Street, Klerksdorp, NW, 2571
Tel: 018 465 4088, Fax: 018 465 4293

Practice Number [redacted] pg 1 of 1

FULL FINAL LABORATORY REPORT - AMENDED

PATIENT: [redacted]

LAB NUMBER: [redacted]

REPORT TO: [redacted]

29/10/2022 (12m 12d) Sex -

Sample Ref: [redacted]
Collected: 10/11/2023 ?
Received: 10/11/2023 21:00
1st Print: 13/11/2023 10:25
Reprint: 28/11/2023 17:10

Ward not stated

Patient Location: Nic Bodenstein Hospital, Ward not stated

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER [redacted]

MICROBIOLOGY

Tel: TB Lab: 018 465 7860, Fax: TB Lab: 018 465 7907

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct)

TB-NAAT: BD MAX MTB/RIF/INH (Direct)

MTB PCR result	Mycobacterium tuberculosis complex detected
Rifampicin (molecular)	Unsuccessful

TB has been detected. The rifampicin testing was unsuccessful. Submit another sample for smear, culture and DST. Please start first line TB treatment and monitor response to treatment.

Authorised by: DC Moncbe (Medical Technologist) BD Max MTB/RIF/INH (direct)

-- End of Laboratory Report --

TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

TSHEPONG LABORATORY
Tshepong Hospital, 41 Benji Oliphant Street, Klerksdorp, NW, 2571
Tel: 018 465 4088, Fax: 018 465 4293

Practice Number 5200296 pg 1 of 1

FULL FINAL LABORATORY REPORT - AMENDED

PATIENT:

LAB NUMBER:

REPORT TO:

08/08/2001 (22y) Sex F

Sample Ref:
Collected: 10/11/2023 ?
Received: 10/11/2023 21:20
1st Print: 13/11/2023 11:15
Reprint: 28/11/2023 17:09

No ward

Tel H:

Patient Location: Jouberton Clinic

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER

MICROBIOLOGY

Tel: TB Lab: 018 465 7860, Fax: TB Lab: 018 465 7907

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct)

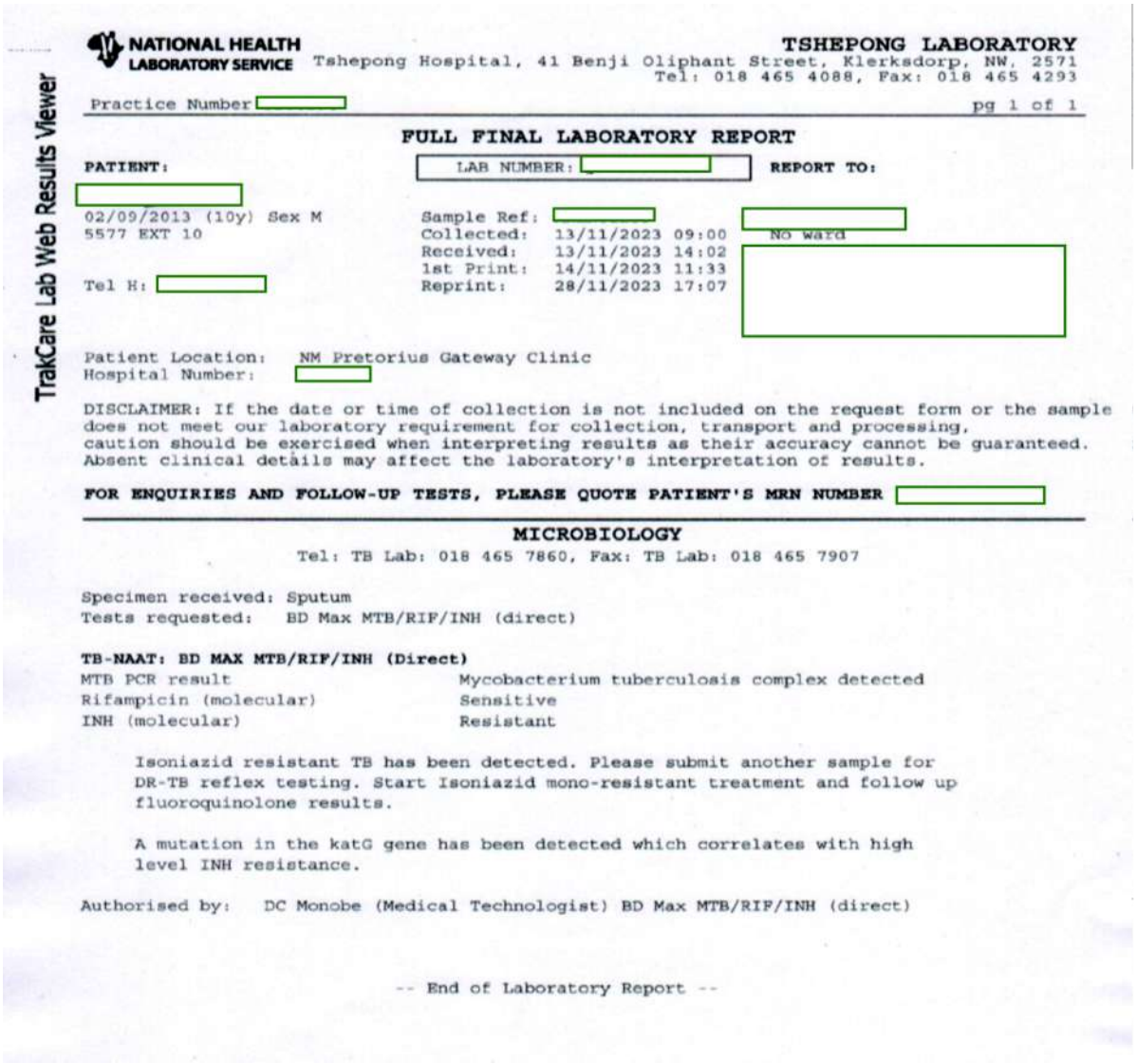
TB-NAAT: BD MAX MTB/RIF/INH (Direct)

MTB PCR result	Mycobacterium tuberculosis complex detected
Rifampicin (molecular)	Sensitive

Rifampicin susceptible TB has been detected. Please submit another sample for baseline microscopy, and initiate appropriate treatment.

Authorised by: DC Monobe (Medical Technologist) BD Max MTB/RIF/INH (direct)

-- End of Laboratory Report --



TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

TSHEPONG LABORATORY
Tshepong Hospital, 41 Benji Oliphant Street, Klerksdorp, NW, 2571
Tel: 018 465 4088, Fax: 018 465 4293

Practice Number [redacted] pg 1 of 1

FULL FINAL LABORATORY REPORT

PATIENT: [redacted]
02/09/2013 (10y) Sex M
5577 EXT 10
Tel H: [redacted]

LAB NUMBER: [redacted]
Sample Ref: [redacted]
Collected: 13/11/2023 09:00
Received: 13/11/2023 14:02
1st Print: 14/11/2023 11:33
Reprint: 28/11/2023 17:07

REPORT TO: [redacted]
No ward

Patient Location: NM Pretorius Gateway Clinic
Hospital Number: [redacted]

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER [redacted]

MICROBIOLOGY
Tel: TB Lab: 018 465 7860, Fax: TB Lab: 018 465 7907

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct)

TB-NAAT: BD MAX MTB/RIF/INH (Direct)

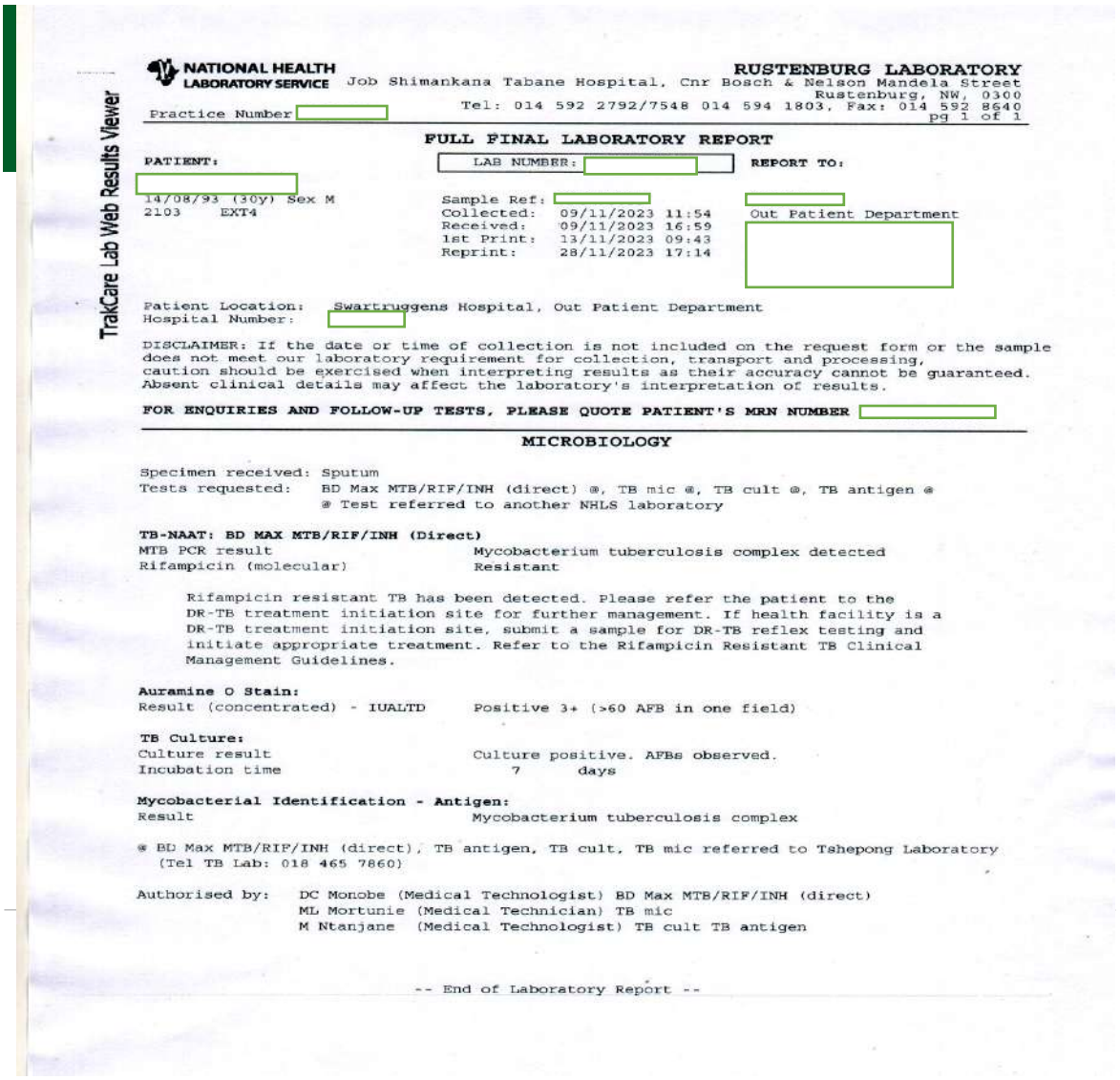
MTB PCR result	Mycobacterium tuberculosis complex detected
Rifampicin (molecular)	Sensitive
INH (molecular)	Resistant

Isoniazid resistant TB has been detected. Please submit another sample for DR-TB reflex testing. Start Isoniazid mono-resistant treatment and follow up fluoroquinolone results.

A mutation in the katG gene has been detected which correlates with high level INH resistance.

Authorised by: DC Monobe (Medical Technologist) BD Max MTB/RIF/INH (direct)

-- End of Laboratory Report --



TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

Job Shimankana Tabane Hospital, Cnr Bosch & Nelson Mandela Street
Rustenburg, NW, 0300
Tel: 014 592 2792/7548 014 594 1803, Fax: 014 592 8540

RUSTENBURG LABORATORY

pg 1 of 1

Practice Number

FULL FINAL LABORATORY REPORT

PATIENT:

LAB NUMBER:

REPORT TO:

14/08/93 (30y) Sex M
2103 EXT4

Sample Ref:
Collected: 09/11/2023 11:54
Received: 09/11/2023 16:59
1st Print: 13/11/2023 09:43
Reprint: 28/11/2023 17:14

Out Patient Department

Patient Location: Swartruggens Hospital, Out Patient Department
Hospital Number:

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER

MICROBIOLOGY

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct) @, TB mic @, TB cult @, TB antigen @
@ Test referred to another NHLS laboratory

TB-NAAT: BD MAX MTB/RIF/INH (Direct)

MTB PCR result	Mycobacterium tuberculosis complex detected
Rifampicin (molecular)	Resistant

Rifampicin resistant TB has been detected. Please refer the patient to the DR-TB treatment initiation site for further management. If health facility is a DR-TB treatment initiation site, submit a sample for DR-TB reflex testing and initiate appropriate treatment. Refer to the Rifampicin Resistant TB Clinical Management Guidelines.

Auramine O Stain:

Result (concentrated) - IUALTD	Positive 3+ (>60 AFB in one field)

TB Culture:

Culture result	Culture positive. AFBs observed.
Incubation time	7 days

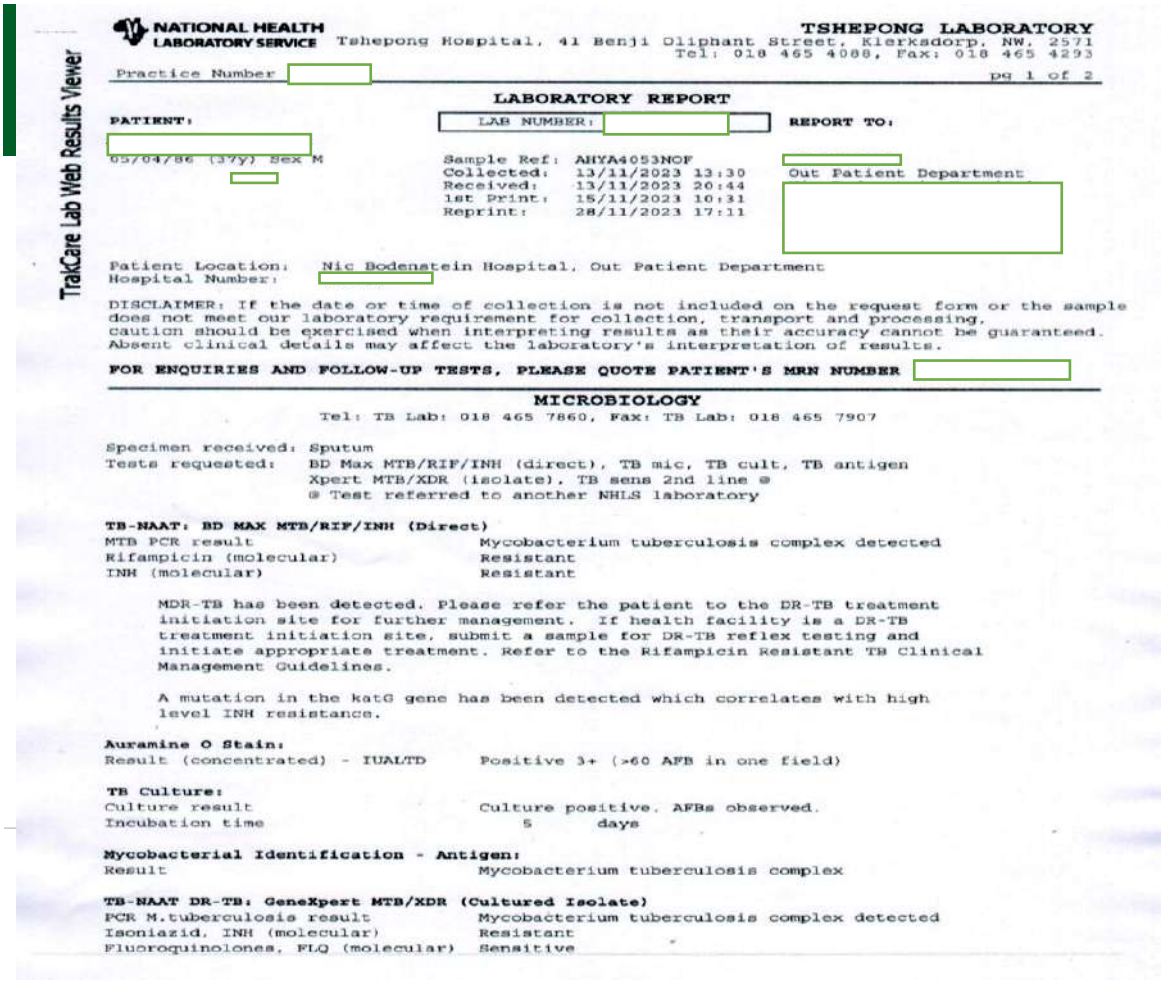
Mycobacterial Identification - Antigen:

Result	Mycobacterium tuberculosis complex

@ BD Max MTB/RIF/INH (direct), TB antigen, TB cult, TB mic referred to Tshepong Laboratory (Tel TB Lab: 018 465 7860)

Authorised by: DC Monobe (Medical Technologist) BD Max MTB/RIF/INH (direct)
ML Mortunie (Medical Technician) TB mic
M Ntanjane (Medical Technologist) TB cult TB antigen

-- End of Laboratory Report --



TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

Tshepong Hospital, 41 Benji Oliphant Street, Klerksdorp, NW, 2571
Tel: 018 465 4000, Fax: 018 465 4293

TSHEPONG LABORATORY

Practice Number

pg 1 of 2

LABORATORY REPORT

PATIENT:

05/04/86 (37y) Sex M

LAB NUMBER:

REPORT TO:

Sample Ref: AHYA4053NOF
Collected: 13/11/2023 13:30
Received: 13/11/2023 20:44
1st Print: 15/11/2023 10:31
Reprint: 28/11/2023 17:11

Out Patient Department

Patient Location: Nic Bodenstein Hospital, Out Patient Department
Hospital Number:

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER

MICROBIOLOGY

Tel: TB Lab: 018 465 7860, Fax: TB Lab: 018 465 7907

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct), TB mic, TB cult, TB antigen
Xpert MTB/XDR (isolate), TB sens 2nd line @
@ Test referred to another NHLS laboratory

TB-NAAT: BD MAX MTB/RIF/INH (Direct)

MTB PCR result	Mycobacterium tuberculosis complex detected
Rifampicin (molecular)	Resistant
INH (molecular)	Resistant

MDR-TB has been detected. Please refer the patient to the DR-TB treatment initiation site for further management. If health facility is a DR-TB treatment initiation site, submit a sample for DR-TB reflex testing and initiate appropriate treatment. Refer to the Rifampicin Resistant TB Clinical Management Guidelines.

A mutation in the katG gene has been detected which correlates with high level INH resistance.

Auramine O Stain:

Result (concentrated) - IUALTD	Positive 3+ (>60 AFB in one field)

TB Culture:

Culture result	Culture positive. AFBs observed.
Incubation time	5 days

Mycobacterial Identification - Antigen:

Result	Mycobacterium tuberculosis complex

TB-NAAT DR-TB: GeneXpert MTB/XDR (Cultured Isolate)

PCR M.tuberculosis result	Mycobacterium tuberculosis complex detected
Isoniazid, INH (molecular)	Resistant
Fluoroquinolones, FLQ (molecular)	Sensitive

TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

TSHEPONG LABORATORY

Tshepong Hospital, 41 Benji Oliphant Street, Klerksdorp, NW, 2571
Tel: 018 465 4088, Fax: 018 465 4293

Practice Number 5200296 pg 1 of 1

FULL FINAL LABORATORY REPORT

PATIENT:

07/05/69 (54y) Sex M

LAB NUMBER:

REPORT TO:

Family Medical Clinic

Sample Ref:
Collected: 30/10/2023 ?
Received: 13/11/2023 08:42
1st Print: 14/11/2023 11:29
Reprint: 28/11/2023 17:10

Patient Location: Tshepong Hospital, Family Medical Clinic
Hospital Number:

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER

MICROBIOLOGY

Tel: TB Lab: 018 465 7860, Fax: TB Lab: 018 465 7907

Specimen received: Sputum
Tests requested: BD Max MTB/RIF/INH (direct), TB mic

TB-NAAT: BD MAX MTB/RIF/INH (Direct)

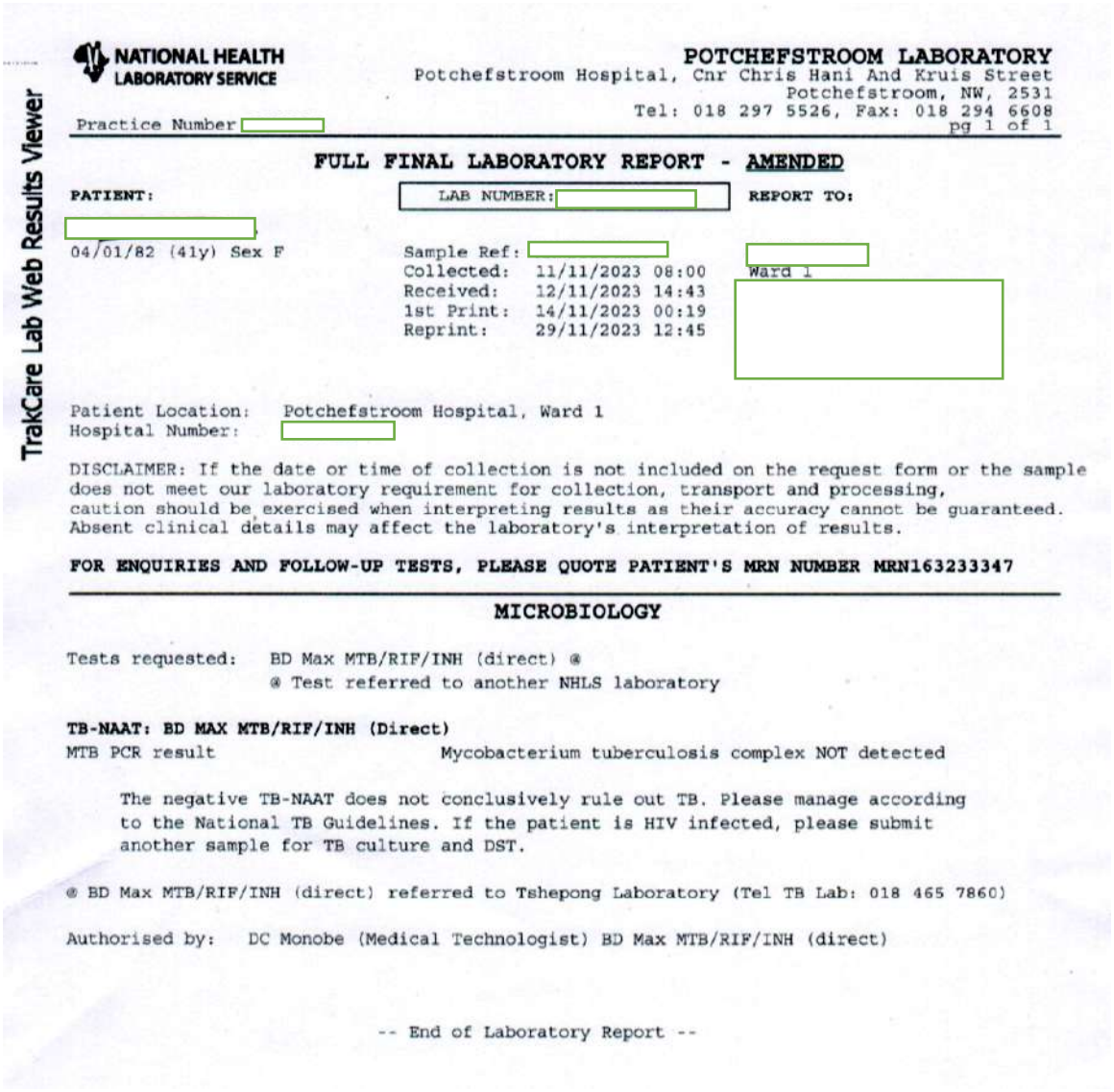
MTB PCR result	Trace
Rifampicin (molecular)	Unsuccessful

Mycobacterium tuberculosis DNA detected at the lowest limit of detection. The rifampicin testing was unsuccessful. Refer to the National TB Guidelines.

Auramine O Stain:
Result (concentrated) - IUALTD Negative (No AFB observed in one length)

Authorised by: DC Monobe (Medical Technologist) BD Max MTB/RIF/INH (direct) TB mic

-- End of Laboratory Report --



TrakCare Lab Web Results Viewer

NATIONAL HEALTH LABORATORY SERVICE

POTCHEFSTROOM LABORATORY
Potchefstroom Hospital, Cnr Chris Hani And Kruis Street
Potchefstroom, NW, 2531
Tel: 018 297 5526, Fax: 018 294 6608
pg 1 of 1

Practice Number

FULL FINAL LABORATORY REPORT - AMENDED

PATIENT:

LAB NUMBER:

REPORT TO:

04/01/82 (41y) Sex F

Sample Ref:
Collected: 11/11/2023 08:00
Received: 12/11/2023 14:43
1st Print: 14/11/2023 00:19
Reprint: 29/11/2023 12:45

Ward 1

Patient Location: Potchefstroom Hospital, Ward 1
Hospital Number:

DISCLAIMER: If the date or time of collection is not included on the request form or the sample does not meet our laboratory requirement for collection, transport and processing, caution should be exercised when interpreting results as their accuracy cannot be guaranteed. Absent clinical details may affect the laboratory's interpretation of results.

FOR ENQUIRIES AND FOLLOW-UP TESTS, PLEASE QUOTE PATIENT'S MRN NUMBER MRN163233347

MICROBIOLOGY

Tests requested: BD Max MTB/RIF/INH (direct) @
@ Test referred to another NHLS laboratory

TB-NAAT: BD MAX MTB/RIF/INH (Direct)
MTB PCR result Mycobacterium tuberculosis complex NOT detected

The negative TB-NAAT does not conclusively rule out TB. Please manage according to the National TB Guidelines. If the patient is HIV infected, please submit another sample for TB culture and DST.

@ BD Max MTB/RIF/INH (direct) referred to Tshepong Laboratory (Tel TB Lab: 018 465 7860)

Authorised by: DC Monobe (Medical Technologist) BD Max MTB/RIF/INH (direct)

-- End of Laboratory Report --

5.8 Urine lateral flow Lipoarabinomannan Assay (Urine LF-LAM)

5.8.1 Definition

Lipoarabinomannan (LAM) is a polysaccharide (i.e. a combination of lipid and carbohydrate).

It is the main component of the mycobacterial cell wall. This compound is released by metabolically active or degenerating mycobacterial cells and appears to be present in people with active TB disease LAM is an antigen (i.e. it is perceived as foreign by the immune system) and therefore triggers an immune response.

It is detectable in the urine after it has been excreted via the kidneys. The detection of the TB-LAM antigen enables the diagnosis of both pulmonary and extrapulmonary TB. The test used to detect LAM is the Determine™ TB LAM Ag Test, manufactured by Abbott and distributed locally by Obsidian Health Pty LTD.

It is a rapid urine-based test which detects LAM in urine and thus enables rapid diagnosis of TB in people living with HIV. It is a point-of-care test (POCT) for the diagnosis of active TB. Point-of-care tests(POCT) refer to tests performed near or at the point of patient care. These tests are performed based on clinical observations to help clinicians promptly diagnose and treat patients.

5.8.2 Strengths and limitations of U-LAM

Table 5.2

Strengths	Limitations
- It is specific for the MTB complex - Short Turnaround Time (TAT) - Detects MTB and RIF Resistance (High sensitivity for RIF Resistance)	- Reduced sensitivity in smear negative cases - Does not detect INH resistance - Itcannotbeusedformonitoring response to treatment

5.8.3 Criteria for the use of LF-LAM In-patient setting

- The test should be used to assist in the diagnosis of active TB in the following categories of people living with HIV.
    - Irrespective of whether TB is suspected or not (i.e. irrespective of signs and symptoms of TB), and
    - Irrespective of the CD4 count, and
    - Irrespective of whether advanced HIV disease (AHD) is present or not.

NB: Sputum for the TB-NAAT test should be collected in parallel.

Out-patient setting

- The test should be used to assist in the diagnosis of active TB in the following categories of people living with HIV:
    - Signs and symptoms of TB (pulmonary and /or extrapulmonary TB), and
    - CD4 cell count ≤ 200 cells/mm^3 or AHD stage 4, or who are seriously ill.

Sputum for the TB-NAAT best should be colleted in parallel

Definition of advanced HIV disease (AHD)

Advanced HIV disease (AHD) is defined as a CD4 cell count of fewer than 200 cells/µL or a World Health Organization Clinical Stage 3 or 4 at presentation for care.

All children with HIV who are aged under 5 years should be considered as having AHD at presentation. Children under 5 years who are stable on ART should not be classified as having AHD.

Stable on ART refers to the following criteria:

- Receiving ART for at least 12 months.
- No adverse drug reactions requiring monitoring.
- No current illnesses and good understanding of lifelong adherence and evidence of treatment success (two consecutive undetectable viral load measures or; in the absence of viral load monitoring, rising CD4 cell counts or CD4 cell counts exceeding 200 $cell/mm^3$ and an objective adherence measure).

Definition of seriously ill patient

Seriously ill patients (adult norms) are defined based on four danger signs:

- respiratory rate of more than 30 breaths per minute
- temperature of more than 39 °C
- heart rate of more than 120 beats per minute
- unable to walk unaided and/or have a low BMI (<18.5) and/or severely underweight or wasted

For children, signs of serious illness include:

- lethargy or unconsciousness
- convulsions
- unable to drink or breastfeed
- repeated vomiting

Other clinical conditions such as body temperature ≥39 °C and age-defined tachycardia and/or tachypnoea can be considered based on clinical judgement.

5.8.4 Test procedure

Watch video: Urine LAM, 12 minutes 54 seconds at https://www.youtube.com/watch?v=F08U1DNSFy8

Preparation of the Testing Station

Table 5.3: Preparation for conducting urine LAM test. Materials required:

Materials required:	**Station Preparation**

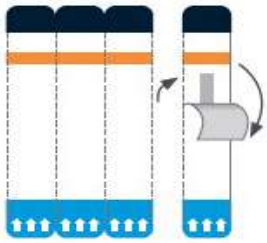
- Test kit with the following:
  - 5 Abbott Determine TB LAM Ag test card (each with 5 test strips, total = 25 strips)
  - Reference scale card
  - A desiccant to keep the contents of the kit dry & stable.
  - Disposable 60µL pipettes
Materials not supplied but required.
- Sterile urine specimen container
- Disposable gloves
- Timer
- Blotting paper sheet
	• Check the condition of the test kit and strips for damage and defects.
	• Check expiry date of the test kit.
	• The test should not be used if:
	  - the packaging is damaged,
	  - test strips are wet,
	  - beyond its expiry date
	• Remove the required test strip and place the remaining ones back into the packaging and reseal.

Collection of urine specimen

Clear instructions must be provided to the patient on the collection of urine Patient instructed to:

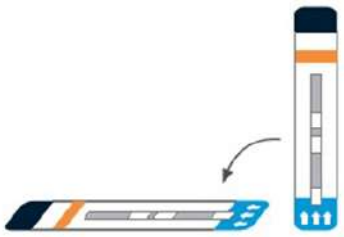
- clean and wipe the urogenital area before collecting urine
- allow the first stream of urine to flow and collect mid-stream urine into the container provided
- wipe the sides of the container and wash hands after collecting urine
- early morning urine is preferred where it is feasible to obtain, i.e., hospital settings

Figure 5.1: Performing the test



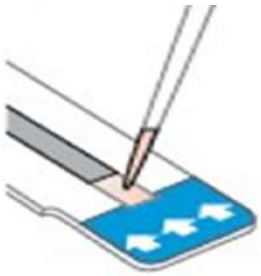
1

Remove the test strip starting from the right by bending and tearing at the perforation.
This is to ensure that the Lot Number on the left side of the card is always available.
Remove the protective foil cover by pulling from the top to expose the test strip.



2

Place the test strip flat on the counter/ table where the test is to be performed facing up.



3

Draw urine from the specimen bottle/ jar using the pipette by squeezing and releasing the upper bulb of the pipette.

4

Place about 60 µL of urine in the white pad marked by arrows (sample pad), by squeezing the upper bulb of the pipette.

Wait for 25 minutes and read the results.

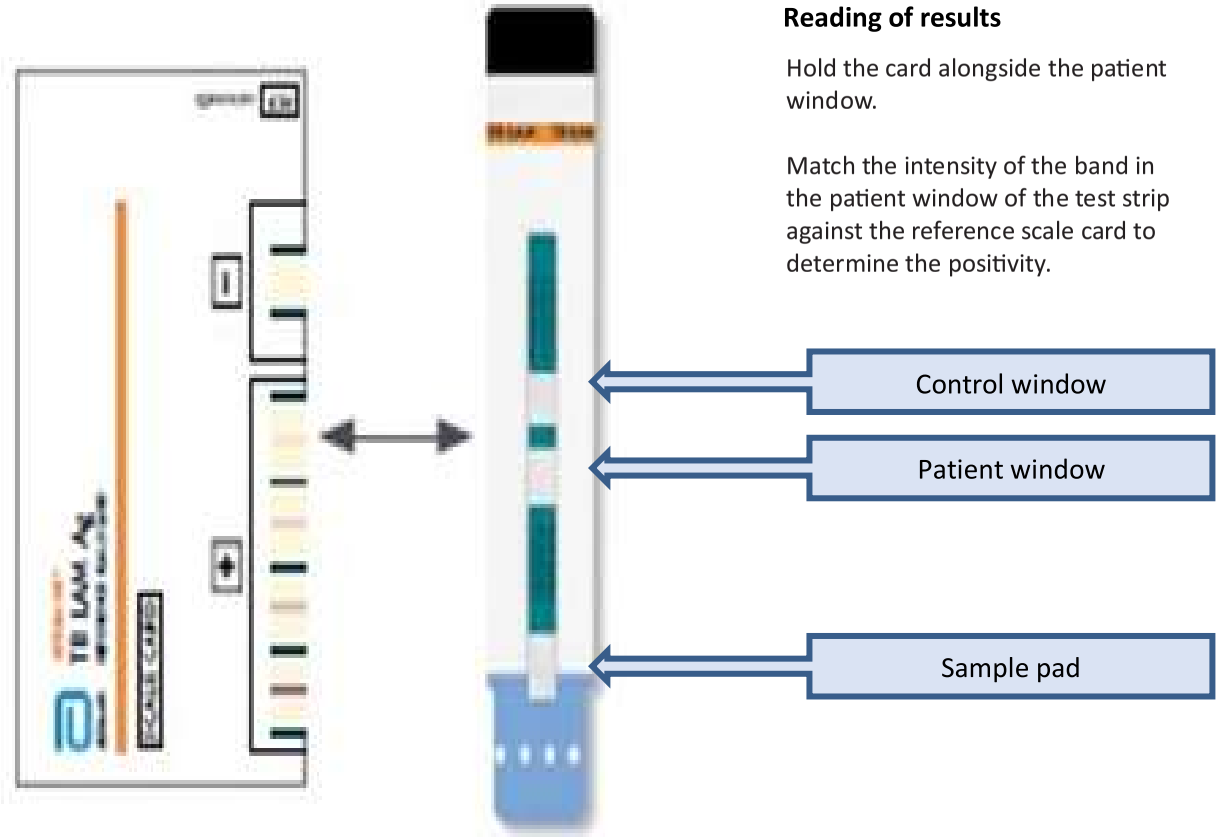
Figure 5.2: Reading of Result

Reference Scale Card

The reference scale card is supplied with all test kits.

It is used to assist in reading the results by holding it next to the result window on the test strip. After use, it must be stored in the sealed test kit pouch and protected from heat and direct sunlight.

It must not be used after the expiry date.



Reading of results

Hold the card alongside the patient window.

Match the intensity of the band in the patient window of the test strip against the reference scale card to determine the positivity.

The results are stable up to 35 minutes. **Do not read after 35 minutes.**

5.8.5 Urine LF-LAM test result Table 5.4: LF-LAM POSITIVE

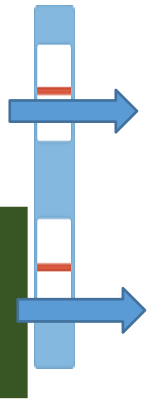
LINE	POSITIVE	LAM ANTIGEN POSITIVE
CONTROL		(Two bars – Control and Patient Bars) Purple/grey bars appears in both the control window (labelled "Control").
		AND
PATIENT		The Patient window (labelled "Patient") of the strip. Colour intensity should be equal to or stronger than any of the coloured bars in the positive range on the reference scale card.

Table 5.5: LF-LAM NEGATIVE

LINE	NEGATIVE	LAM ANTIGEN NEGATIVE
CONTROL		(One bar – Control Bar) One Purple/grey bar appears in the control window of the strip (labelled "Control").
PATIENT		No purple/grey bar appears in the Patient window of the strip (labelled 'Patient").

Table5.6: LF-LAM Invalid

LINE	INVALID	LAM ANTIGEN INVALID
CONTROL		(No Control Bar) If there is no purple/ grey bar in the control window of the strip, even if a purple /grey bar appears in the patient window of the strip, the results is invalid and the test should be repeated.
PATIENT		If the problem persists, contact Technical Support or your local Abbott representative.

Table 5.7: LF-LAM Equivocal/Indefinite

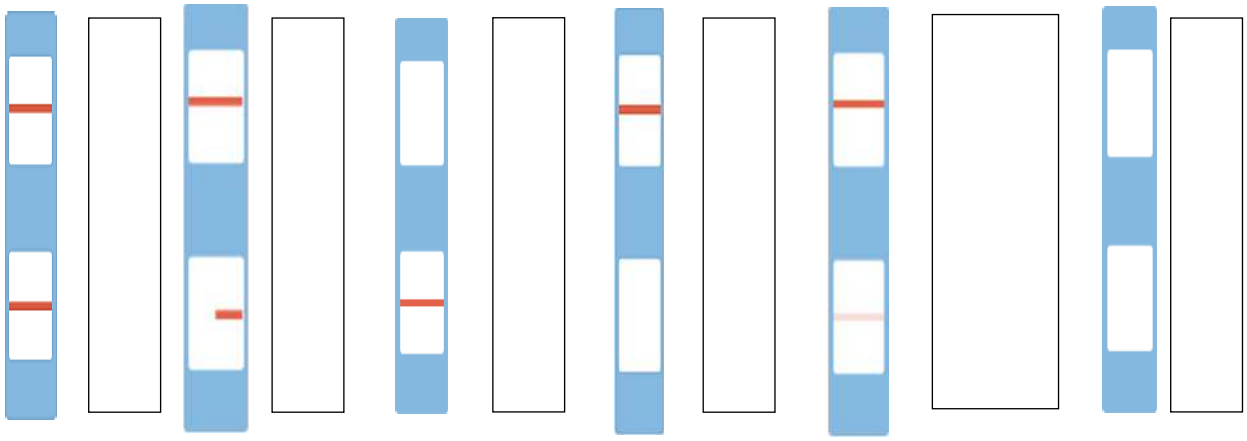
LINE	INDEFINITE	LAM ANTIGEN EQUIVOCAL/INDEFINITE
CONTROL PATIENT		(One bar – Control Bar) One Purple/grey bar appears in the control window of the strip (labelled "Control") with unclear or incomplete (broken line or dot) purple /grey bar in the Patient window of the strip (labelled "Patient"). OR The colour of the bar in the Patient window is lower than coloured bars in the Positive range on the reference scale card. For a better clinical decision, the test should be repeated. Alternatively, collect a new urine sample in the following day from the patient and test. First or early morning urine is recommended.

Individual exercise 1

Below are the test strips after conducting urine LF_LAM test.

Right the result for each strip on the cell next to the strip.

Indicate what action should be taken.



Top window in all the strip is the control Note window and the bottom window is the patient window

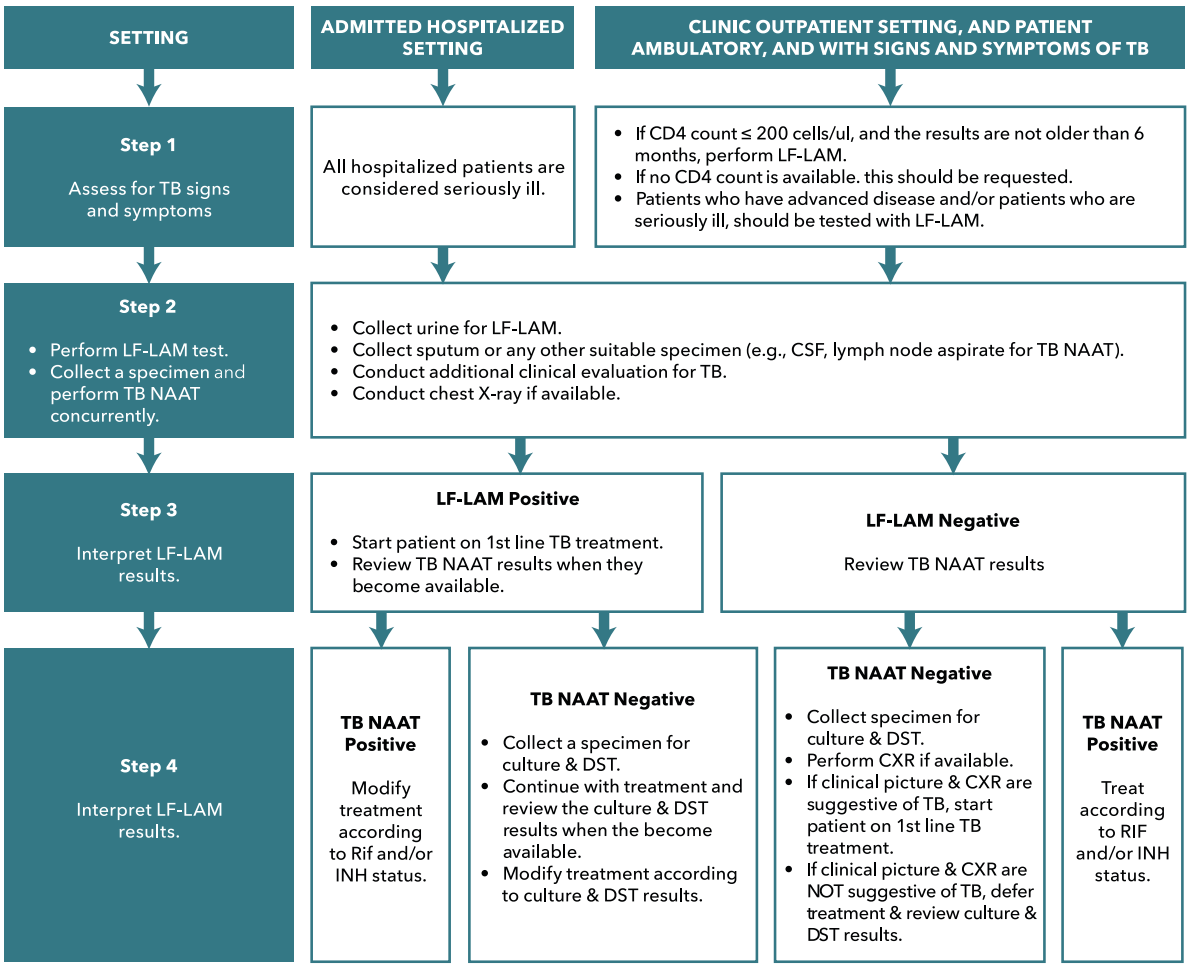
Acting on the LF-LAM results LF-LAM Positive

- Start the patient on TB treatment- first-line TB treatment.
- Review the TB NAAT results once they become available.
- If MTB detected, review the resistance pattern.
  - If Rifampicin sensitive, continue with first-line TB treatment (Regimen 1 or 3)
  - If Rifampicin resistant, stop DS-TB treatment, record patient as RR-TB and refer to DR-TB treatment site for initiation of second-line TB treatment.
- If MTB not detected, collect a sputum specimen for culture and DST.
  - Continue with first line TB treatment, review the culture and DST results once they become available.
  - If TB culture positive, review the resistance results.
  - If drug susceptible, continue with first-line TB treatment.
  - If drug resistant, stop DS-TB treatment, record patient as RR/MDR-TB, refer to the DR-TB treatment site for initiation of second-line TB treatment.

LF LAM negative

- Review the TB NAAT results once they become available.
  - If MTB Detected, review resistance pattern.
    - If Rifampicin sensitive, start the patient on first-line TB treatment (Regimen 1 or 3).
    - If Rifampicin resistant, refer to DR-TB treatment site for initiation of second-line TB treatment.
  - If MTB not detected, collect a sputum specimen for Culture and DST.
    - Clinically assess the patient and conduct chest X- ray, if available.
    - If abnormal chest X-ray suggestive of TB or TB is clinically suspected, treat with first-line TB treatment:
    - If the patient is clinically stable and chest x-rays normal, follow up for culture and DST result.
  - Review the culture and DST results
    - If culture positive and sensitive to Rifampicin and Isoniazid, start first-line TB treatment.
    - If culture positive and Rifampicin/multidrug resistant, refer to DR-TB treatment site for initiation of second line TB treatment.

Table 5.8: Summary of action steps to take



Individual exercise 2

3 elements to consider at PHC level before conducting LF-LAM test:_____

_____

Define advanced disease for HIV positive adults and children_____

_____

Define seriously ill for HIV positive patients_____

_____

True or false

- LAM test is conducted together with sputum collection for TB NAAT.
- Negative urine LAM means the patient does not have TB.
- Positive urine LAM results means that you can initiate a patient on TB treatment.
- Wait for TB NAAT results before starting patient on treatment in case the TB NAAT results comes negative.

5.9 Tuberculin Skin Test

5.9.1 Definition of Tuberculin Skin Test (TST)

The Tuberculin Skin Test (TST) is also known as the Mantoux Test. It is a skin test to determine whether a person is infected with a bacterium, Mycobacterium and is the most reliable skin test available. The test involves injecting tuberculin purified protein derivative (PPD) into the skin.

5.9.2 Indications

- To diagnose latent infection in children and adults
- To support the diagnosis of TB in children

The test requires:

- 2 units of tuberculin purified protein derivative PPD-RT23 2TU or
- 5 units of PPD-S 5TU

5.9.3 Tuberculin Skin Test – Procedure

- A single-dose tuberculin syringe and a short 27-gauge needle with a short bevel must be used.
- Draw up 0.1ml of PPD into the syringe.
- Clean an area of skin in the mid anterior section of the forearm.
- The PPD is injected between layers of skin (intradermal).
- Keep the needle almost parallel to the skin, with the bevel pointing upwards during insertion.
  - It is important to ensure that the injection goes into and not under the skin.
- A small papule should form at the injection site; if it does not, the PPD has been injected too deeply and the test should be repeated at a different site.

5.9.4 Reading of results

- The reaction to the test at the site of the injection is measured 48-72 hours later by noting the widest transverse point across the edges of the raised, thickened area.
- This area of induration and not redness is measured.
- To help measure accurately, mark the edges of the induration at the widest point with a pen and measure the exact distance between the two points in millimetres.
- There are two cut off points for defining a positive tuberculin reaction: >5 mm and >10 mm, based on the risk i.e. immune status of the patient.
- For high-risk patients such as those who are HIV positive, malnourished, with severe illness (immunosuppressive disease or on immunosuppressive treatment), a reading ≥ 5mm is considered positive.
- For all other patients, a reading of ≥ 10mm is considered positive.

Table 5.9: Reading TST

Reading the Tuberculin Skin Test		
Immune Status	HIV positive, malnourished, severe illness	Others (including previous BCG)
Diameter of induration in positive test	≥ 5 mm	≥ 10 mm

Table 5.10: TST result interpretation

Positive TST	Negative TST
A positive TST indicates infection with TB, but not necessarily TB disease. - In a child under 5 years or HIV-infected child of any age, a positive skin test indicates recent infection and is a risk factor for progression to disease. - In the presence of a history of a TB contact, signs and symptoms of TB and chest x -ray changes, a positive tuberculin skin test is suggestive of TB disease in children.	A negative TST does not exclude TB because various conditions may cause a false negative reaction such as: - HIV infection - Malnutrition - Severe viral infections (e.g. measles, chicken pox) - Cancer - Immuno -suppressive drugs (e.g. steroids) - Severe disseminated TB

Action on TST Results

The following patient groups must be assessed for TPT eligibility if they have a positive TST and no symptoms or signs of TB

- Children under the age of 5 years who are contacts
- HIV positive children of any age

Child contacts with a positive TST, signs and symptoms of TB, chest x-ray abnormalities suggestive of TB disease or both, must be treated for TB

Children with a negative TST, signs and symptoms of TB, chest x-ray abnormalities suggestive of TB disease or both, must be treated for TB

Individual Exercise 3

Which of the following patients have a positive TST reaction? Circle the best answer(s)

a. Phindile Mthonti $2^{6}/_{12}$ yrs. old, HIV positive, 8 mm induration Positive
b. Dakalo Makhuvha, 18 months old, 7mm induration
c. Avhavhudzani Khoza 4 yrs. old, 0 mm induration
d. Bina Thebe girl, HIV unknown, 3yrs old, 13 mm induration
e. Joele Mlambo 5yrs, old, HIV positive, 6mm induration
f. Mulweri Ndau 2yrs old, 9 mm of induration

Individual Exercise 4

Patient	Reason for testing	Investigation and Action to be taken results
Mr Mkhize, 35 years old, male	Presenting with persistent cough for 1 month and loss of weight. Completed TB treatment 19 months ago.	MTB detected, Rif susceptible
Ms Dineo Mokoena, 18 years old, female	Asymptomatic, HIV positive, pregnant, first antenatal visit. No previous history of TB treatment.	MTB detected, Rif sensitive
Nkule, 23 years old, female	Asymptomatic, HIV positive, pregnant, first antenatal visit. History of TB within the past 2 years.	TB NAAT result - Trace
Mr Larry Smith, 47 years old male.	HIV Positive, Last Positive count = 150. Cough, lost weight in the past month and has fever. No previous history of TB treatment.	CD4 U-LAM
Ms Nandy Chule, 4 years old female	Asymptomatic contact. Index patient started on regimen1, 2 weeks ago.	
Mr Goodman Grootboom, 66 years old male	Presented with cough, loss of appetite and general body malaise, for 3 weeks. Treated for TB 3 years ago.	MTB Trace detected

6. TREATMENT, SIDE EFFECTS AND DRUG INTERACTION

Module overview:
The module covers treatment regimens, side effects and drug interaction.
Learning outcomes:
By the end of this session, participants should be able to:

- List the aims of TB treatment.
- Explain the properties of TB drugs.
- Describe the properties of each individual TB drug.
- Explain the TB Regimen.
- Describe the standardised regimen for new and previously treated patients.
- Describe the side effects of TB treatment.
- Explain other drug interaction with TB treatment.

6.1. Baseline clinical evaluation

An appropriate clinical assessment should be made at the start of tuberculosis treatment to identify other existing comorbidities and to ensure appropriate comprehensive individualised care for each patient.

Table 6.1 Baseline evaluation for patients with TB

Investigations		Recommended frequency
Microscopy	All patients with MTB detected results	Baseline, 7 weeks and 23 weeks
Height	All patients	Baseline
Weight	All patients	Baseline and at treatment collection intervals
Body mass index	All patients	Baseline
HIV test	Patients with unknown HIV status	Baseline
Blood glucose	Urine glucose and ketones (All patients)	Baseline
	Blood glucose (symptomatic patients)	Baseline and monthly for diabetic patients
Pregnancy test	Women of childbearing age, presenting with history of amenorrheoa and not on contraception	Baseline
Alcohol use screening	Patients with a history of alcohol use	Baseline
Mental health screening	All patients	Baseline
Liver function tests	In patients with a history of liver disease, excessive alcohol use	Baseline
Serum creatinine	In patients with a history of kidney disease	Baseline, monthly

6.2. Properties of TB treatment

The aim of TB treatment is to:

- cure the patient of TB
- decrease transmission of TB to others
- prevent the development of acquired drug resistance
- prevent relapse
- prevent complications of TB
- prevent death

Properties of TB treatment

TB drugs are bactericidal and bacteriostatic. They differ in the ability to act against the various population of bacilli found in TB lesions, metabolically active bacilli, semi-dormant bacilli (persisters), and dormant bacilli (that may become active). Some TB drugs act best in an acid environment, others better in alkaline environment. Bacilli can be found in extracellular spaces where the PH is usually neutral or alkaline and intracellular where the PH is acidic.

Table 6.1: Properties of TB drugs

Properties of the individual TB Drugs				
Drugs	**Drug Property**	**Target Bacilli**	**pH**	**Site of Action**
Isoniazid (H)	High potency Bactericidal after 24hrs - kills 90% bacilli in first few days of Rx	Rapid and intermediate growing bacilli	Alkaline and Acid media	Intra and extracellular
Rifampicin (R)	High potency Bactericidal within 1 hour. Most effective sterilising agent.	All populations including dormant bacilli	Alkaline and Acid media	Intra and extracellular
Pyrazinamide (Z)	Low potency Bactericidal Achieves its sterilising effect 2-3 months.	Slow growing bacilli	Acid media	Intracellular bacilli only macrophages
Ethambutol (E)	Low potency Bacteriostatic Minimises the emergence of drug resistance.	All bacterial population	Alkaline and Acid media	Intra and extracellular

6.3. Standardised treatment/drug regimen for DS-TB

A drug regimen is a prescribed systematic form of treatment for a course of drug(s). Treatment regimens for TB have a standard code. Each TB medicine/drug has an abbreviation i.e. Isoniazid (H); rifampicin pyrazinamide (Z); ethambutol (E).

The three regimens used in the country are:

- Regimen 1: For new and previously treated adults and children >8 yrs. and >25kg.
- Regimen 3A: For children <8yrs and < 25kg with uncomplicated TB disease.
- Regimen 3B: For children <8yrs and <25kg with complicated TB disease.

A TB treatment regimen consist of two phases:

- 2 months of intensive phase with a Fixed Dose Combination (FDC) of the following drugs: Rifampicin, Isoniazid, Pyrazinamide and Ethambutol (RHZE).
- 4 months of Continuation Phase (CP) phase in the FDC of the following drugs: Rifampicin and Isoniazid (RH). RH has a sterilizing effect on remaining bacilli and prevents subsequent relapses.

Treatment is taken for 7 days. The recommended standard treatment is 6 months which is equal to 168 doses, 56 doses intensive phase and 112 doses continuation phase. It is important to ensure the patient receives the correct number of doses even if this takes longer than 6 months, i.e., if a patient misses a dose(s) for any reason, these doses should still be taken, thereby 'lengthening' the treatment time but not the actual number of doses.

Treatment is prescribed according to the weight. Patients during intensive phase must be weighed monthly, and the dose adjusted according to their current weight. Monitoring of response to treatment is important. Good response to treatment will be reflected by: clinical improvement, weight gain, or/and conversion of smear from positive to negative.

Patient education

The key to controlling the spread of TB in a community is to treat the patients with infectious TB disease and cure them at the first attempt. Effective management of TB disease depends on standardized and correct treatment regimen for the duration of 6 months.

Education for patient with TB on treatment should include the following:

- Take tablets on an empty stomach. This means at least 30 minutes before food or 2 hours after food. They are best taken at least 30 minutes before breakfast.
- If it irritates your stomach, you may take the tablets with a light meal.
- Swallow the tablets whole, with water.
- Take all your tablets together each day, as a single dose.
- You should usually take all the day's tablets at the same time each day and only stop taking them if your doctor tells you to.
- If you forget to take your tablets, take them as soon as you remember on the same day. If it is nearly time for the next dose, then take the next dose as usual. Do not take a double dose to make up for the forgotten tablets.
- Antacids used for indigestion can make TB medicine work less well. Give TB medicine at least 1 hour before or 2 hours after taking antacids.
- Do not give this medicine to children.
- If you feel the effect of your medicine is too weak or too strong, do not change the dose yourself, but ask your doctor.

1. TB Treatment Regimen 1

Regimen 1 should be used for children more than 8 years, weighing 25kg or more, adolescents and adults.

Table: 6.2 Regimen 1

Pre-treatment body weight kg	2 months intensive phase given daily	4 months continuation phase given daily	
	RHZE (150,75,400,275)	RH (150,75)	RH (300,150)
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70.9 kg	4 tablets		2 tablets
>70.9 kg	5 tablets		2 tablets

Individual exercise 1 1st Visit

Fani Dumakude is a 52-year-old male patient, diagnosed with TB two days ago and is now at the facility for initiation of treatment. Fani weighs 57kg.
How many RHZE tablets will Fani take per day?.....
What is the return date for Fani?.....

REGIMEN AND DOSAGES

Treatment start date: | | | | | | | | |

Regimen 1 | | Regimen 3 | | Other: | | Specify: |

Medicine	RHZE 150/75/400/275	RHZ 75/50/150	RH (60/60)	R	H	Z	E
No. of tablets/ dosage per day							

Body weight at start of intensive phase: | | kg

Month	Date																												
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

√ = patient took medication
x = patient did not take medication
— = medication collected for self administration or supervision elsewhere

2nd Visit

Fani reports back at your facility after 27 days. Treatment is well tolerated. No side effects reported. Give Fani another month of treatment and record on the treatment card
Total number of tablets given to Fani?.....

Treatment of TB in children

The treatment of tuberculosis in children < 25 kg is covered in the training course "Management of tuberculosis in children".

2. Minor Side effects

Table 6.7: Minor side effects

Side effects	Most likely causative drug	Management
Anorexia, nausea, abdominal pain	Rifampicin Ethionamide	- Exclude other possible causes e.g. Alcohol, Non-steroidal anti -inflammatory drugs (NSAIDs). - Ask patient about history of gastritis, gastric ulcers, gastro -oesophageal reflux, pancreatitis, etc. - Give TB treatment with small meals or just before bedtime (do not give on an empty stomach). - Advise the patient to stagger the tablets, swallow one tablet at a time with small sips of water in between tablets, over longer period of time. - Note: Take required dose within 30 minutes. - Give antacid and anti- emetic. - If the above fails, refer.
Orange /red coloured urine	Rifampicin	- Reassurance. - Patients should be told when starting treatment that this may happen and is normal.
Joint pains	Pyrazinamide	- Reassure the patient that it is a self-limiting condition.

Side effects	Most likely causative drug	Management
		- Low dose pain medication can be given e.g. Paracetamol and Ibuprofen. - If severe, refer.
Tingling / Burning / numbness sensation in the hands and feet	Isoniazid Ethionamide	- Prevention. - In high- risk groups, give Pyridoxine 25 mg daily for prevention. - Alcohol abusers. - Pregnant (Never exceed the recommended dose). - Diabetic or epileptic. - Management. - Pyridoxine 50-75mg daily. - HIV+ Recommended dose is 100mg.

3. Major Side Effects

Table 6.8: Major side effects

Side effects	Most likely causative drug	Management
Visual impairment/ loss (other causes excluded). Blurred vision (decrease in the "sharpness" of objects) "spots "present in the patient's field of vision. Red/green colour blindness. Difficulty in reading.	Ethambutol Ethionamide	- Stop treatment immediately - Refer
Medicine induced Hepatotoxicity Signs and symptoms: Loss of appetite, nausea, jaundice, dark urine, discoloured stools, pain and tenderness in the upper right abdomen.	Isoniazid Rifampicin Pyrazinamide Ethionamide	- Rule out other causes e.g. Excessive alcohol use, other medication the patient is taking, pre -existing liver disease and viral hepatitis - Stop all medicines the patient is taking (TB treatment, cotrimaxazole, ART) - Refer
Confusion	Isoniazid, Rifampicin, Pyrazinamide	- Stop TB drugs/FDC - Refer
Generalised purpura, shock	Rifampicin	- Stop Rifampicin/FDC - Refer

Rash

Table 6.9: Rash

All TB drugs can cause rash. The management depends on the severity	
Mild itching rash	- Give antihistamine - A topical cream may be added
Petechial rash	- Mainly due to Rifampicin - Conduct Platelet count, if below normal range (150,000-450,000 per microliter), stop Rifampicin and exclude from regimen - Monitor platelet count until it returns to normal
Erythematous rash with fever	If rash improves, the drugs can be re-introduced one by one every 2-3 days: - Start with Rifampicin (potent least likely cause) - Follow by Isoniazid - Then Pyrazinamide - And Ethambutol Monitor signs and symptoms. If rash occurs, last drug added should be stopped

4. Shared side effects between TB and HIV

Table 6.10: TB&HIV

Side effects	Most likely causative drug	Management
Nausea and vomiting	Didanosine, Zidovudine (AZT), Protease Inhibitors (PI)	Pyrazinamide
Hepatitis	Nevirapine, Efavirenz protease inhibitors when dose is increased to overcome Rifampicin induction	Rifampicin, Isoniazid, Pyrazinamide
Neuropsychiatric side effects	Efavirenz	Isoniazid,
Renal toxicity	Tenofovir	Rifampicin
Rash	Nevirapine, Efavirenz	Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and

6.4. Drug Interaction

Drug interaction refers to the possibility of one drug may altering the pharmacological effects of another drug given concomitantly. The net result may be enhanced or diminished effects of one or both drugs, or the appearance of a new effect that is not seen with either drug alone. If not sure of possible drug interaction with any other medicine that the patient is taking, always check with pharmacist.

Before initiating a client on TB treatment (and at every subsequent visit), it is important to take a thorough medication-related history to identify any potential drug-drug interactions. Ask about TB medications, treatment for Non-Communicable Diseases (hypertension, diabetes, epilepsy, mental illness) and any other prescribed medication. Also ask about over the counter (OTC) medications and traditional remedies.

1. TB and contraception

Women who are on enzyme inducing drug (e.g. rifampicin) should not use progestin subdermal implants (Implanon).

Use IUCDs or DMPA

The effectiveness of combined oral contraceptives may be impaired by rifampicin Could be used together with condoms if women prefer this method.

Women who are on rifampicin and already have the progestin subdermal implants (Implanon) inserted should be covered with another non-hormonal contraceptive method (IUCD or condoms) for the duration of their TB treatment.

2. TB and ART

Dual treatment of both HIV and active TB in co-infected patients has various implications which includes:

- The timing of ART initiation
- Drug selection in clients who are not yet on ART when TB treatment is initiated
- Drug levels due to significant drug interaction that reduce ART concentration in the blood
- Adherence due to increased pill burden
- Side effects due to overlapping toxicities, e.g. hepatic toxicity

Clinicians should provide integrated TB and ART management at clinical consultation visits. Failure to combine care leads to increased visits and significantly increases the risk of disengagement.

6.4.2.1. TB/HIV Drug interaction

Table 6.11: Co-treatment of HIV and active TB in neonates, infants, children, adolescents and adults

TB/HIV co- infection impacts on ART in a number of ways. It affects:

1. **The timing of ART initiation**
2. **Drug selection** in clients who are not yet on ART when TB treatment is initiated
3. Drug levels, due to significant **drug interactions** that reduce ART concentration in the blood
4. **Adherence** due to increase pill burden
5. **Side effects** due to overlapping toxicities e.g. hepatic toxicity

Clients who are not yet on ART when TB treatment is initiated

- Children and adolescents should initiate ART with a DTG-containing regimen, with boosting of DTG as explained below.
- Adults should initiate ART with either:
  - a DTG -containing regimen, with boosting of DTG as explained below, or
  - an EFV-containing regimen, provided the client is ART treatment -naïve. EFV has no significant drug interaction with rifampicin and has the benefit of being a once-daily regimen which supports adherence.

Clients who are already on ART when TB treatment is initiated

- All clients who are already on a DTG-containing regimen when TB treatment is initiated should continue the DTG-containing regimen whilst also taking TB treatment, with boosting of DTG as explained below.
- Clients who are already virally suppressed on an EFV-containing regimen when TB treatment is initiated should continue the EFV-containing regimen whilst also taking TB treatment. The EFV-containing regimen should be continued until two weeks after TB treatment is completed. Thereafter, EFV can be switched to DTG.

! Clinicians should provide integrated TB and ART management at clinical consultation visits. Failure to combine care leads to increased visits and significantly increases the risk of disengagement

Drug interaction with DTG and Rifampicin-containing TB Treatment

Rifampicin-containing TB treatment has significant drug interaction with all paediatric ART regimens, as well as with adult/adolescent regimens containing DTG:

	2.0 kg	3 kg	30 kg
ART Regimen	**Neonates** AZT + 3TC + NVP	**Infants and Children** ABC + 3TC + DTG	**Adolescents and Adults** TDF + 3TC + DTG
Significant drug interaction	**! Rifampicin + NVP**	**! Rifampicin + DTG**	
Measures to counteract drug interactions with rifampicin	**Seek expert advice**	**Boosting of DTG required** In adults and adolescents, the dosing frequency of DTG should be increased to 50mg 12-hourly. If on TLD FDC, then add DTG 50mg 12 hours after TLD dose. For DTG-boosting in children, refer to drug dosing chart	

Continue boosting the ART regimen until 2 weeks after stopping rifampicin

Drug interactions with Protease inhibitors, e.g. Lopinavir/ritonavir

Every effort should be made to switch clients to DTG-containing regimens. However, during the transition process, some clients may still be on PI-containing regimens and may also require TB treatment. Rifampicin cannot be given with ATV/r or DRV/r. Significant drug interactions between LPV/r and rifampicin should be managed as follows:

LPV/r tablets: Double-dose LPV/r tablets in adults, adolescents and children able to swallow whole LPV/r tablets. Tablet must not be crushed, broken or chewed. If the client is unable to tolerate LPV/r at double doses, consult one of the "Helplines".

LPV/r solution or pellets or 4 in 1 (ABC/3TC/LPV/r): Super-boosting with additional ritonavir powder: maintain standard LPV/r dose but add additional ritonavir twice daily as per "Drug dosing chart". If no powder is available, consult an expert for a suitable alternative. Ritonavir powder has a shelf -life of 36 months. Note that ritonavir 100mg tablets must not be crushed, broken or chewed

6.4.2.2. Integration of TB/HIV visits

- Clinicians should provide integrated TB management at clinical consultation visits. Failure to combine care leads to increased visit schedules and significantly increases the risk of disengagement and loss-to-follow-up (LTF).
- This schedule is for a standard DS-TB treatment (Rx) regimen consisting of 2 months of intensive phase Rx (IP) and 4 months of continuation phase (CP) Rx after a negative smear at the end of the IP.
- This schedule applies to a client already on ART when diagnosed with drug-sensitive TB. A client diagnosed with HIV and TB can also benefit from 2 months' supply of ART and TB continuation phase to support adherence and retention.

Table 6.12 Integrated visit schedule for a client on ART who develops DS-TB

Integrated visit schedule for a client on ART who develops DS-TB (not in RPCs)		Months (M) on TB treatment (Rx)						
		Intensive Phase (IP) (months 1-2)				Continuation Phase (CP) (months 3-6)		
		TB M0	TB M1 (4 completed weeks)	7 wks	TB M2 (8 completed weeks)	TB M4 (16 completed weeks)	23 wks	TB M6 (24 completed weeks)
Integrated TB/ART clinical consult	TB screening as part of routine care	TB diagnosis and TB Rx initiation	Clinician-managed care at facility		Assess smear conversion and transition to CP of TB Rx, if smear result is negative	Clinician-managed care at facility		Confirm TB Rx completion, assess for RPCs enrolment
Investigations	TB NAAT and any other investigations as clinically indicated	Review result		**Smear**	Review result		**Smear**	Review end-of-Rx result
ART/TB script	Script ART for 1 month	Combined script for 1 month of IP TB Rx and ART	Combined script for 1 month of IP TB Rx and ART		Combined script for 2 months** of CP TB Rx and ART	Combined script for 2 months** CP of TB Rx and ART		If eligible for RPCs: RPCs ART script for 6 months
ART-TB drug supply dispensed by facility	Dispense ART for 1 month	Dispense 1 month of IP TB Rx and DTG boosted ART	Dispense 1 month of IP TB Rx and DTG boosted ART		Dispense 2 months of CP TB Rx and 2 months DTG boosted ART	Dispense 2 months of CP TB Rx and 2 months DTG boosted ART		Dispense 3 months of ART
Ask client to return:	If client has TB symptoms or is unwell, ask client to return in 5-7 days for review*	After 4 weeks for clinical review	After 3 weeks for sputum smear	**After 1 week for smear results**	After 8 weeks for clinical review	After 7 weeks for end of Rx smear	**After 1 week for smear results**	If eligible and enrolled in RPCs: return for next ART supply at RPCs pick-up point after 3 months

6.4.2.3. Timing of ART for TB/HIV co-infected patients

Table 6.13 Timing of ART

Indication	Action
Diagnosis of drug -sensitive (DS) TB at a non -neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis)	Defer ART initiation as follows: • If CD4 < 50 cells/ μL – initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated • If CD4 ≥ 50 cells/ μL – initiate ART 8 weeks after starting TB treatment • In pregnant and breastfeeding women (PBFW) initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated. Defer ART for 4-6 weeks if symptoms of meningitis are present.
Diagnosis of drug -resistant (DR) TB at a non -neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis)	Initiate ART after 2 weeks of TB treatment, when the client's symptoms are improving, and TB treatment is tolerated
Diagnosis of DS-TB or DR-TB at a neurological site (e.g. TB meningitis or tuberculoma)	Defer ART until 4-8 weeks after start of TB treatment

Note: Clients already on ART should NOT have their treatment interrupted upon diagnosis of TB

7. PATIENT EDUCATION AND ADHERENCE TO TREATMENT

Learning outcomes:
By the end of this session, participants should be able to:

- Explain patient education.
- Describe the content to be included in patient and family education.
- Explain the importance of effective communication with patients.
- Define adherence.
- Explain factors that influence treatment outcome.
- Explain the role of a patient in successful treatment.

7.1. Patient Education Definition

Patient education is the process by which healthcare workers impart information to patients and their families that will alter their health behaviour and health status. Education is provided to encourage and empower patient to adhere.

Patient education and counselling sessions During each session
Sessions can be provided individually or as a group:

- The attitude of the counsellor or healthcare worker providing counselling is extremely important in supporting adherence.
- Each counselling session should start with an introduction.
- The counsellor or healthcare worker providing counselling should use their counselling skills to build trust with the patient and ensure that the patient is comfortable.
- Create a warm environment and promote patient's openness by establishing language reference and informing about their right to confidentiality.
- Show your appreciation to the patient for attending scheduled appointment at facility.
- Ask questions to help understand the patient's situation and make time to listen carefully to their answer and discuss misunderstandings regarding treatment.
- Encourage and provide time for the patient to ask questions and discuss their concerns.
- Discuss immediate concerns and help patient decide who in their social network may be available to provide immediate support.
- Provide referrals to other services if needed.

At the end of the visit:

- Provide encouraging messages explaining the next steps on treatment at the end of the session.
- Discuss any further questions or concerns that the patient may have.
- Schedule a follow-up visit for a date and time the patient is available, for next clinical or treatment supply visit date.
- Write the date of the follow-up visit in the patient's treatment folder, TB treatment card and facility appointment register.
- Encourage patient to adhere to treatment and return to facility as scheduled.
- Inform the patient that they will be traced if they miss appointments and obtain consent for patient to be visited at home or to be called. Confirm the patient's contact details.
- Provide IEC materials to the patient, if available, after making sure that the patient understands the information in the IEC material in their language.
- Provide health facility telephone numbers for patient to contact if necessary.

7.2 Adherence counselling session

Content to be included in patient and family education

Examples of questions to understand the patient's current knowledge about TB:

- What do you understand about tuberculosis?
- What do you think causes TB? How is it spread?
- Do you know of anyone who had TB? What happened to that person?
- What have you heard about curing TB?

Asking this question may assist you to:

- Tailor the messages to the needs of the patient.
- Build on accurate information that the patient already knows and believes about the disease.
- Concentrate on giving new information.
- Correct wrong beliefs and misperceptions.

Inform patients and their families about TB disease, treatment, adverse events following treatment, infection prevention and importance of sputum examinations. Correct any myth or misinformation the patients may have, e.g. a patient may believe that TB is caused by the “evil spirit” and cannot be cured. The initial messages for this patient should focus on the causes of TB, prevention and the fact that it can be cured with TB medicines.

Effective communication

Effective communication should begin when the healthcare workers (CHWs) engage with the patient for the first time and during subsequent visits. Every engagement with a patient from the time of diagnosis and throughout the course of treatment until the treatment is completed, is an opportunity to provide information and support. HCWs must communicate with patients and families clearly preferably in their local language.

Creating good rapport with patients:

- Speak slowly enough to be understood. Do not rush through instructions.
- Use a kind tone of voice and choose words that are caring rather than accusing. For example, if a patient misses a day: Do not say: “You missed treatment yesterday, do you want your whole family to catch TB?” Instead, say: “I missed you yesterday. What happened?”
- Demonstrate empathy with the patient if there are problems.
- Assess the barriers to adherence and discuss strategies with the patient on how to overcome them.
- Help the patient to find solutions. Solutions may involve arranging transportation, talking with the patient's family or employer.

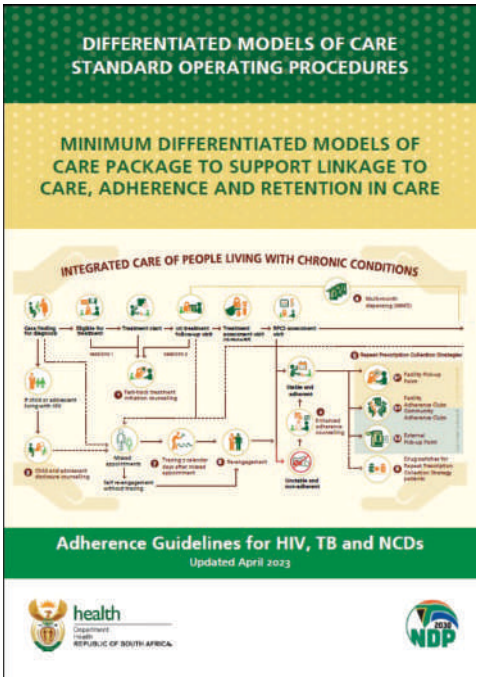
Encourage patients to ask questions:

- Make sure that the patient feels comfortable enough to ask questions. After giving instructions or an explanation, pause and ask, “Do you have any questions? I know this is a lot of information at once.”
- Patients may be timid and concerned about appearing uneducated. Or they may be nervous and simply want to leave the health facility in a hurry.
- It may take courage for them to ask questions.
- Praise patients for asking questions and answer them thoughtfully and carefully. For example, say: “I'm glad you asked that question....” “Good question. ”

Adherence

Definition of adherence

Adherence means the extent to which a person's behaviour corresponds with agreed recommendations from a healthcare worker in respect to taking medication, following a diet and/or implementing lifestyle changes.



Objectives of adherence guidelines

- **to strengthen access to appropriate services and interventions to improve clinical outcomes**
- **to assist service providers to ensure that people with chronic diseases are linked to care, retained in care and supported in adhering to treatment**
- **to address client and service-provider barriers**

Differentiated care approach

A differentiated approach to care, known as Differentiated Models of Care (DMOC), is recommended, which aims to improve adherence and retention in care through a patient-centred approach. Longer duration of treatment, i.e. multi-month dispensing to reduce patient burden and encourage continued participation in treatment, should be prioritised. Repeat prescription collection (RPC) strategies are ideal for those already participating in this model of care.

Exercise 1:

- Go through the patient adherence plan, annexure 3.
- Work in groups of 3s, taking turns in different roles, i.e., a nurse, patient and an observer in a role play.
- Using the patient adherence plan, counsel a newly diagnosed patient starting TB treatment.

8. MONITORING RESPONSE TO TREATMENT

This module provides an overview on how response to treatment is monitored.

Learning Outcomes:

At the end of this module, participants will be able to:

- Explain the difference between clinical monitoring and bacteriological monitoring.
- Describe the clinical monitoring and management of a patient throughout intensive phase.
- Describe the clinical monitoring and management of a patient throughout continuation phase.
- Describe the management of patients interrupting treatment for:
  - less than 1 month
  - 1-2 months
  - 2 months and more

8.1. Monitoring response to treatment

Monitoring of response to treatment is important for clinical care. Patient with bacteriological confirmation of PTB must be assessed clinically and bacteriologically. Patients diagnosed with TB NAAT must have baseline smear results and followed up bacteriologically. Patients with smear –positive or smear –negative are monitored by smear examination. Patients diagnosed without bacteriological confirmation (u-LAM, chest x-rays, TST or other tests and based on clinical assessment) monitored clinically – improvement of clinical signs and symptoms, weight gain.

1. **Bacteriological monitoring**
   - One 'on spot' sputum specimen is taken after diagnosis with TB NAAT for baseline smear microscopy
   - One 'on spot' sputum specimen is taken at the end of week 7 for smear conversion
   - One 'on spot' sputum specimen is taken at the end of the 23rd week for confirmation of cure
   - There should be no interruption of treatment whilst the smears are evaluated
   - Timely collection of sputum is important, and collection and result dates captured in the patient record

The table below summarises the bacteriological monitoring of patients.

Table 8.1: Bacteriological monitoring

Timing of test	Aim	Action	Comments
End of intensive phase			
One week before the end of the 2 months intensive phase of treatment (at 7 weeks)	To determine smear conversion a sign of good clinical progress. To guide the healthcare worker on whether to change the patient to continuation phase of treatment or extend the intensive phase	If negative, change to the continuation phase of treatment at the end of the 8th week of intensive phase treatment. Register the patient as "negative"	This means the patient is responding well to treatment. Educate and counsel patient about importance of treatment compliance

		If positive, check for treatment adherence, re -assess patient clinically 1) Conduct culture and DST. Change to the continuation phase. 2) Register the patient as "positive" 3) Review the drug susceptibility results when available 4) Address treatment adherence by counselling the patient and identifying a treatment supporter where necessary	This indicates the following: 1) That the initial phase of therapy was poorly monitored, and treatment adherence was poor. 2) That there is a slow rate of improvement due to extensive TB disease or high bacillary load at diagnosis. 3) That the patient may have resistance to the other TB drugs i.e. Isoniazid or may have been re -infected with a drug resistant strain. 4) The patient may have another condition or taking other medication that affects the absorption or effectiveness of the TB drugs
End of continuation phase			
One week before the end of the 4 months	To determine the outcome of treatment for the patient.	If negative Stop treatment at the end of the 24th week of treatment. Allocate outcome.	Educate the patient about TB prevention and healthy lifestyle.
Continuation phase (at 23 weeks)		If positive Stop TB treatment. Register patient as "treatment failure" Conduct culture and DST for first line pyrazinamide and second line drugs Review the results when available. If drug susceptible , re-start TB treatment, counsel the patient and provide adherence support.	This indicates the following: 1) That the patient was re-infected with a sensitive or resistant strain 2) The treatment during the continuation phase was unsupervised and patient compliance was poor
		If drug resistant , refer to the MDR-TB treatment initiation facility for assessment and treatment	

Patients remaining positive at 6 months			
Aim		**Action**	
To determine further management treatment, of the patient treatment		- **If drug susceptible, re-start TB counsel the patient and provide support** - **If drug resistant, refer to the MDR-TB treatment initiation facility for assessment and treatment**	
Continuation phase		If positive Stop TB treatment. Register patient as "treatment failure" Conduct culture and DST for first line pyrazinamide and second line drugs Review the results when available. If drug susceptible , re-start TB treatment, counsel the patient and provide adherence support. If drug resistant , refer to the MDR-TB treatment initiation facility for assessment and treatment	This indicates the following: 1) That the patient was re- infected with a sensitive or resistant strain 2) The treatment during the continuation phase was unsupervised and patient compliance was poor
Patients remaining positive at 6 months			
Aim		**Action**	
To determine further management treatment, of the patient treatment		- If drug susceptible, re -start TB counsel the patient and provide support - If drug resistant, refer to the MDR-TB treatment initiation facility for assessment and treatment	

1. **Clinical monitoring**

- EPTB and clinically diagnosed patients must be monitored clinically over the duration of treatment period.
- Bacteriological monitoring should also be accompanied by clinical monitoring.
- Weight is a useful indicator of clinical improvement therefore it should be monitored during the follow up visits
  - Refer TB patient to the doctor within a week if losing weight
  - Adjust the treatment dosage on continuation phase
  - Assessment of TB symptoms and signs must be conducted during the follow up visits:
    - Refer to the doctor or next level of care if symptoms are worsening or not improving
- Side effects to medicines must be monitored regularly:
  - Any side effect should be noted and attended to
  - Adverse events form is completed
- HIV testing for status negative if HIV status unknown:
  - Provide counselling and test for HIV to ensure that patients know their status by end of TB treatment. HIV positive TB patients must be started on ART, following ART guideline.
- Adherence:
  - Review patient treatment card/green card
  - Conduct pill count

8.2. Management of treatment interrupters

1. **Minimising treatment interrupters**

- Early detection of patients who interrupt treatment is essential in preventing loss to follow up
  - When a patient doesn't keep a scheduled appointment
  - A healthcare worker must call, enquire about the patient using the patient contact details provided
  - Send the tracer team member or community healthcare workers to the patient's home as per address provided
  - Use next of kin or employer contact details to contact the patient if available
- On patient retrieval
  - Find out why the patient interrupted treatment and address patient concerns/ challenges
  - Jointly develop an action plan to address the problem

2. **Management of patients who interrupt treatment for less than 1 month**

- Trace the patient
- Establish the cause for interruption of treatment
  - Address problems or concerns and counsel the patient
- If interruption occurred during the intensive phase,
  - add the missing doses before changing to continuation phase
- If interruption occurred during the continuation phase
  - add the missing doses at the end of the continuation phase

Table 8.2: Treatment interruption

Management of patients who interrupted for 1-2 months			
Action	**TB NAAT Results**	**Action 2**	
- Trace the patient - Establish the cause for interruption of - Address the problem or concerns - Provide adherence counselling - Collect sputum for TB NAAT - Continue treatment - Review TB NAAT results.	MTB detected and Rif sensitive	- Continue treatment and add the missed doses at the end of the treatment phase	Monitor until treatment
	MTB Detected and Rif resistant	- Stop treatment - Register patient as RR- TB. - Refer to DR -TB treatment initiating site for further management	Follow up to ensure that the patient has been successfully referred

Patient who interrupted treatment for 2 months or more (LTFU)			
- Trace the patient. - Establish the cause for interruption of treatment. - Address the problem or concerns and provide counselling. - Collect sputum for TB NAAT. - Do not start treatment, wait for the results	MTB detected and Rif sensitive	- Register as "Treatment after loss to follow up" - Re-start Regimen 1	- Monitor as usual until treatment is completed.
	- MTB detected and Rif resistant	- Register patient as RR- TB. - Collect sputum specimen for DRTB Reflex testing - Refer to DR - TB treatment initiating site for further management.	Follow up to ensure that the patient has been successfully referred.

3. Management of clinically diagnosed patients who interrupted treatment for 1-2 months

- Every effort must be made to collect a sputum specimen in patients who were clinically diagnosed, i.e., diagnosed made based on other tests or based on clinical assessment and EPTB.
- If patient cannot expectorate, continue treatment, and add the missed doses at the end of the treatment phase.
    - o Provide adherence counselling
    - o Educate patient on side effects of medicines
    - o Clinically monitor the patients closely

Appendix 1

PHC RISK ASSESSMENT TOOL

TUBERCULOSIS INFECTION PREVENTION AND CONTROL RISK ASSESSMENT FORM FOR CLINICS AND COMMUNITY HEALTH CENTRES

FACILITY DATA SHEET

Facility Identification	
Facility Name:	
Facility Type:	
Physical Address	
Building Name:	
Street Number:	
Street Name:	
Suburb:	
Town/City:	
Location	
Province:	
District:	
Local Authority	
Information Source / Lead facility representative	
Name:	
Designation:	
Contact Numbers:	
Email Address:	
Data Control	
Lead Assessors Name:	
Designation:	
Contact Numbers:	
Email:	
Assessment Date:	

Section 1: Facility Staff Details

Facility Staff Complement	

Section 2: Facility Patient/ Occupancy Data

Patient Visits per Quarter (Number of Patients):						**Year:**	
First Quarter		**Second Quarter**		**Third Quarter**		**Fourth Quarter**	
Total visits (all):		Total visits (all):		Total visits (all):		Total visits (all):	
No. screened		No. screened		No. screened		No. screened	
No. TB presumptive		No. TB presumptive		No. TB presumptive		No. TB presumptive	
New Susceptible TB		New Susceptible TB		New Susceptible TB		New Susceptible TB	
New Drug Resistant TB		New Drug Resistant TB		New Drug Resistant TB		New Drug Resistant TB	
Total Drug Resistant TB		Total Drug Resistant TB		Total Drug Resistant TB		Total Drug Resistant TB	

Section 3: Staff Screening for TB

3.1. Is there a TB screening programme in place for facility staff?	Yes	No	
3.2. Are base-line chest X-ray undertaken for facility staff?	Yes	No	
3.3. Is sputum collected for all identified facility staff?	Yes	No	
3.4. Is completing a screening questionnaire part of the program?	Yes	No	
3.5. How frequently are the facility staff screened?	Every		Months

Section 4: TB Among Staff

4.1.1. How many staff members have been diagnosed with TB in the past 12 months?		
4.1.2. How many staff members have been diagnosed with TB in the past 3 years?		
4.1.3. Did you submit occupational illness report(s) to the compensation commission?	Yes	No
4.1.4. Have you investigated the case(s) of occupational illness & took corrective actions?	Yes	No
4.1.5 Do you have access to occupational health services and advice?	Yes	No
4.1.6. Are you aware of support services available to help you with staff health matters?	Yes	No

Section 5: Management of Infection Control (IC) Program

5.1. TB Infection Control Policy	Yes	No
5.1.1. Is there a facility -specific infection control policy for airborne infections?	Yes	No
5.1.2. Do (all) staff have access to the infection control policy?	Yes	No
5.1.3. Are the HCWs being routinely trained on TB IC practices and requirements?	Yes	No
5.1.4. Is there someone appointed in writing to be in-charge of infection control?	Yes	No
5.1.5. Is there a functional infection control committee?	Yes	No
5.1.6. Are the infection control committee members appointed in writing?	Yes	No

5.2. Is the IC Policy supported by an IC Plan that allows implementation of the following?

5.2.1. Screening of all patients arriving at the hospital?	Yes	No
5.2.2. Separation of patients with presumptive TB or confirmed TB disease?	Yes	No
5.2.3. Fast-tracking of patients with presumptive TB or confirmed TB disease?	Yes	No
5.2.4. Appointment of person(s) to assist in triaging & fast-tracking patients with presumptive TB?	Yes	No
5.2.5. Provision of surgical masks to patients?	Yes	No
5.2.6. Health education and cough etiquette?	Yes	No
5.2.7. Inclusion of respiratory protection programme?	Yes	No
5.2.8. Inclusion of an open window policy (If not relying fully on mechanical ventilation)?	Yes	No
5.2.9. Appointment of open window marshals with access to “open window registers”?	Yes	No
5.2.10. Integration of TB screening with HCT and TB/HIV in general?	Yes	No
5.2.11. Conducting a TB risk assessment frequently	Yes	No
5.2.12. If yes, when was the last assessment undertaken?	Date	

Comments:

Section 6: Turn-Around Times (average number of days it takes for the following)

6.1. Collection of patient sputum until laboratory test results are returned to the facility?		Days
6.2. Time between receipt of tests until initiation of anti-tuberculosis treatment?		Days
6.3. Time taken by laboratory to provide outcome of culture results.		Days

Comments:

Section 7: Additional Comments

Comments:

Section 8: Summary of Recommendations

Comments:

ENVIRONMENTAL CONTROLS

Section 1: Sputum Collection

○ Where is sputum collection undertaken? (Tick all that apply)	
○ An inside room or other (toilet, consulting room, ward etc.)	
○ Designated, purpose made outside area for sputum induction	
○ No designated area (outside etc.) – Just an open space	
○ Local exhaust ventilation booth	

Comments:

Section 2: Natural Ventilation

2.1. If facility relies on natural ventilation, are the spaces open directly to the outside?	Yes	No
2.2. If naturally ventilated, are all openable windows always open?	Yes	No
2.3. Does the facility have “open window stickers and register”?	Yes	No

Comments:

Section 3: Mechanical Ventilation (where applicable)

3.1. Are air changes per hour measured in this facility of unit?	Yes	No
3.2. Are any of the air changes per hour measured below 12 ACH?	Yes	No
3.3. Are ventilation systems regularly checked, maintained & maintenance logbook kept?	Yes	No
3.4. Are these results readily available?	Yes	No

Comments:

Section 4: Air Disinfecting Systems by Upper Room UVGI (where applicable)

4.1. Were the UVGI units installed using an electrical engineer? (if by supplier state No).	Yes	No
4.2. Were the UVGI units validated for operation by an independent authority?	Yes	No
4.3. Are the UVGI units regularly checked and maintained?	Yes	No
4.4. Are each of the UVGI unit performance results recorded in maintenance logs?	Yes	No
4.5. Has the staff been trained to ensure safe operation of the UVGI units?	Yes	No

Comments:

Section 5: Additional Comments

Comments:

Section 6: Summary of Recommendations

Comments:

PERSONAL PROTECTITIVE EQUIPMENT

Section 1: Respiratory Protection Programme(RPP)

○ Does the facility has a respiratory protection programme (RPP)	Yes	No
○ Are respiratory protection equipment used in this setting for all healthcare workers who may be at risk?	Yes	No
○ If YES, specify manufacturer, model and specific application below.		

Manufacturer:	
Class: (NIOSH – N95 or CEN-FFP2)	
Serial Number (e.g. TC number for NIOSH approved respirators)	
Describe the practice and method of respirator donning, use and storing:	

○ Is respiratory -protection training conducted for HCWs?	Yes	No
○ If yes, is it conducted every six months?	Yes	No
○ After direct observation of selected staff, can they perform fit checking?	Yes	No
○ Have the relevant health -care workers undergone fit -testing for respirator use?	Yes	No

Comments:

Section 2: Summary of Recommendations

Comments:

Annexure 2

INITIATION COUNSELLING GUIDE

Explain the purpose of your session:

- Acknowledge that as facility staff you are there to support patients in this process.
- Explain that the first step of the adherence plan is to receive education on illness and treatment.
- Explain to patients that you will assist them by discussing together any barriers they or those close to them may have and to assist them in creating an individualised adherence plan to help them take their treatment correctly.

Education on illness and treatment: individual or group

- Provide education on illness and treatment for patient's condition.
- Be open and alert to any personal difficulties and struggles with aspects of the information.
- Ask questions to assess understanding.

Identify life goals

Explain the reason for discussing life goals

- Ask patient to think about things that make them want to stay healthy and to live fully.
- Ask them to think about the important people in their lives, what projects or goals they have in their future.
- Ask them to identify 3 specific things such as things they really want that others may not even know about. It may be goals common to many of us for example, getting married, go to school or work or taking care of my family or very specific to the person.

Identify support system

Assist the patient to identify support system by asking the following questions:

- Who could support you in taking your treatment?
- Do you have access to other support structures such as church, school and friends?
- How important do you think it is to disclose your health status?
- Would you be willing to be visited at home or contacted by phone?
- Please confirm the telephone number where we can reach you. We will not disclose the reason for our call if someone else answers.
- Who will help you to keep track of your next appointment?

Plan for future appointments

Assist the patient to plan for future appointments by asking the following questions:

- How will you travel to your appointments?
- What will you do if something prevents you from coming to your appointment such as no money for transport, raining when you usually walk, taxi strike or a sick child or any other reason?

Assess the readiness of the patient to start treatment

Ask the patient the following questions to assess if they have any concerns regarding starting treatment

- How do you feel about starting TB treatment?
- Do you have any concerns regarding starting TB treatment? Provide patient with information that will help them correct the misconceptions or myths about treatment.

MEDICATION SCHEDULE

Ask the patient the following:

- According to your schedule, what would be the best time for you to take your treatment?

MANAGING MISSED DOSE

Ask the patient the following:

- What will you do in case you forget to take a dose?

Advise patient to take the treatment as soon as they remember.

ADHERENCE STRATEGIES

Ask the patient the following:

- What reminder strategy will you have in place to avoid forgetting treatment?

Advise on setting watch, cell phone alarm, using pill box or ask someone to remind to take treatment.

STORING MEDICATION AND EXTRA MEDICATION DOSES

Ask the patient the following:

- Who are you worried may see you taking treatment? Offer possibilities such as maybe your children or a neighbour; invite them to share why this is so.
- What safe place could you identify to store your treatment?
- In case you do not have access to your treatment at the time you are supposed to take it, how can you always carry 1 or 2 doses with you?

DEALING WITH SIDE EFFECTS

Remind the patient side effects can occur and are a normal part of adjusting to treatment. Ask patient:

- Do you know about possible side effects?
- What will you do if you are experiencing side effects?

Reassure and support patient explaining that:

- People react differently to medicines.
- Like all medicines, the medicines for treating TB can have side effects, however, severe side effects are rare.
- You may notice, orange discolouration of urine and possible other body fluids and it is normal
- Report to a health facility, if you think you are having any reaction to your treatment. Adverse reaction may include:
    - loss of appetite accompanied by nausea, vomiting or yellowing of the skin or eyes
    - persistent tingling, numbness, or burning of hand or feet
    - persistent weakness, fatigue or abdominal tenderness
    - blurred vision or change in vision

STEP 11: EXPLAIN TREATMENT PATHWAY AHEAD

Explain to the patient that if they take their treatment well, they will be eligible for longer treatment supply and easier collection systems.

STEP 12: PLAN FOR TRAVELS

Ask the patient the following:

- Do you plan to travel in the coming weeks or months?
- What would you do to make sure you can continue your treatment if you go away?
- What could you do in case you have an unplanned trip and cannot come to the facility?

Inform patients that:

- Things can happen suddenly, try to remember the best approach would be to come to the facility before travelling to inform them of your travel location and length of time away so that you can receive a referral letter and sufficient treatment supply.
- If the trip is not planned and you cannot come to the facility, it is important to go to the nearest facility in the travel area as soon as you arrive to make sure you can access treatment there. It is important to carry evidence of your condition and evidence of the treatment you are taking.
- While referral/transfer letters make it easier for the staff at the new facility, it is important to know that the new facility may not require you to obtain a referral/transfer letter before providing treatment to you. Treatment should be provided on the day you present at the new facility to ensure you do not interrupt treatment.

STEP 13: DEALING WITH SUBSTANCE AND TRADITIONAL MEDICINE USE

Explain that:

- Ideally, it is better to moderate alcohol or substance consumption when you are on treatment. But if you have difficulties limiting your consumption to 1 or 2 drinks, it is still important to make sure that you do not forget to take your treatment.

Ask the patient:

- In case you are going to drink alcohol or use drugs, what could you do to make sure you remember to take your treatment?

Support the patient to make a plan by assessing if someone could help make sure they take their medication in case they use drugs or alcohol or if they should rather take it at another time when they are less likely to forget.

- If the patient is planning to use alcohol or drug, it might be more appropriate to take the treatment before as this decreases the risk to forget to take it.
- If the patient recognises that they have a substance abuse disorder, propose referral to a specific support structure (refer to list of organisations who could assist with psychosocial support). Bear in mind that passing judgment is not helpful. It is important to adopt a supportive attitude.

Explain to patient that it is better not to use traditional medicines that could interfere with the treatment. If the patient takes traditional medicine, they should make a plan with the clinician to still take their treatment.

Encourage patients to think about their three reasons to stay healthy to re-motivate them when they experience difficulty in taking their treatment.

TREATMENT PATHWAY

- Check the patient folder for type of TB and treatment duration and explain to the patient.
- For drug sensitive TB with 6 months' treatment duration explain:
    - You will be taking 4 drugs in combination for the first two months (intensive phase) and if the treatment is working change to two drugs in combination (continuation phase) for the remaining 4 months of treatment.
    - A follow-up sputum test called a smear microscopy will be done at 7 weeks on treatment.
    - If the smear microscopy is negative and you are well, it means the treatment is working and you can change from intensive to continuation phase of TB treatment. You can ask and the nurse/doctor could offer longer treatment supply to reduce the number of follow-up visits to the clinic.
    - Another follow-up sputum test will be taken at 23 weeks on treatment and reviewed a week later. If again negative, you have successfully completed TB treatment and it can be stopped.
    - If the smear microscopy is positive, further tests will be done and dependent on the results, you may require changes to the TB drugs prescribed. Your clinician will provide more detailed information in this regard.

- **Explain the importance of continuing and adhering to treatment until completing the course of treatment.**
- **Advise patients with TB, on how to prevent infecting other people by opening windows and covering their mouth when coughing.**
- **Agree on a goal with the patient to complete the TB treatment and be cured.**

Annexure 3

PATIENT ADHERENCE PLAN

Name and Surname:

FTIC Session 1 after chronic disease education session (date):
Adherence step 1: education on HIV ☐ TB ☐ Hypertension ☐ Diabetes ☐ Other ☐……..……
Adherence step 2: Life goals: My motivations to stay healthy are: (1)…… (2)…… (3)…….. I will maintain a healthy lifestyle by ☐ adopting healthy eating habits ☐ getting regular exercise ☐managing my stress
Adherence Step 3: Patient Support system Agree for home visit: Yes ☐ No ☐ Preferred means of contact: SMS ☐ WhatsAapp ☐ Phone call ☐ Other ☐…… Who can support me in my treatment: ☐ Family ☐ Friends ☐ Work ☐ School ☐ Church ☐ Other:
Adherence Step 4: Getting to appointments I will come to my appointments by: walk public transport own transport If I face a difficulty to come (money, transport, etc.), my alternative plan will be to ask for assistance from: family friends neighbour other …… I will inform clinic I am unable to come to set appointment and request for an alternative appointment
Adherence step 5: My readiness to start treatment I feel ready and will start treatment: Yes I am ready today Yes No but will be on …… (insert date) I do not feel ready and would like to discuss more with: peer family member other ……
Adherence Step 6: Medication schedule The best time for me to take my treatment is: Morning Afternoon Evening
Adherence step 7: Managing missed doses If I miss a dose, my plan is: (1) to take treatment as soon as I remember
Adherence Step 8: Reminder strategies To remind me to take medication I will use: watch cell phone alarm pill box buddy other ……...
Adherence Step 9: Storing medication and extra doses I will store my medication in: Safe place …… Far from reach of children I will carry extra supply in: a bag pill box other:…..…… I will keep it in my: handbag pocket other:…..……
Adherence Step 10: Dealing with side-effects If I experience side effects, I will: Refer to treatment adherence pamphlet Inform clinic if side effects do not go away or are too worrying
FTIC Session 2 (date):
Adherence Step 11: Understanding the treatment pathway ahead of me if I take my treatment well I understand the options for multi month treatment supply and simplified collection available after one normal assessment result.
Adherence Step 12: Planning for trips *If I have some trips planned, before going away I will:* Inform health facility before travelling to receive referral letter and treatment Get enough supply of treatment for trip *In case I cannot come to the facility before going away:* I will report to the nearest health facility in the travel area as soon as I arrive to get access to treatment Carry evidence of my condition and evidence of the treatment I am taking
Adherence Step 13: Dealing with substance use *My plan to make sure I take my medication if I used alcohol or drugs is:* To make sure I take treatment before starting to use drugs or alcohol Arrange for someone to remind me to take treatment in case I am intoxicated
Education on assessment: Viral load Sputum HbA1c BP Other: ……..……..…… I understand that I can access multi-month treatment supply and simplified collection if my results are normal **Patients signature** …… **Date of signature** ……
EAC Session 1 (date):
EAC Session 2 (date):

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