National Tuberculosis Management Guidelines 2014

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

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This document was compiled by Directorate:

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Private Bag X828
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Designed and printed by Fishwicks PTA
012 349 1070

ISBN: 978-1-920031-82-4

FOREWORD

Tuberculosis and HIV/ AIDS are the drivers of morbidity and mortality in the country. Therefore more effort must be put into strategies that help us to:

1) reduce transmission of infection in the communities,
2) diagnose DS-TB and DR-TB early,
3) initiate treatment in all patients diagnosed with TB early,
4) retain patients in treatment and care until completion of treatment and
5) prevent TB in people lining with HIV by initiating all eligible HIV positive people on ART and Isoniazid preventive therapy.

Implementing all these strategies in combination will help us as a country to attain the Millennium Development Goals.

To this end, we have introduced new rapid diagnostic tests for drug susceptible and drug resistant TB, additional and new medicines for treating MDR and XDR-TB and are scaling up ward based outreach teams as part of PHC re engineering to provide care and support for patients at home and promote healthy lifestyle.

Health care professionals play a pivotal role in the management of TB patients and we remain grateful for their dedication and hard work. I would like to invite all partners and individuals working in the health sector to join us, as we strive to attain our vision of a long and healthy life for all South Africans.

Minister of Health
Dr Aaron Motsoaledi

ACKNOWLEDGEMENTS

These guidelines are meant to provide guidance to professional health care workers on the management of people with Tuberculosis as well as those co-infected with HIV. The main changes in these guidelines include;

- Targeted screening intervention to increase detection
- The use of Xpert MTB RIF in diagnosing pulmonary and extra pulmonary TB
- The revised definitions and treatment regimen for retreatment patients
- Management of adverse drug events
- ART initiation and follow up of patients on both ART and TB medicines

The development of these guidelines has been collaboration between the National, Provincial Department of Health and technical partners. The Department of Health acknowledges the technical support provided by the WHO and the inputs of all the partners who were involved in the development of these guidelines.

Director General for Health
Ms M P Matsoso

LIST OF ABBREVIATIONS

AFB	Acid-Alcohol Fast Bacilli
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
BCG	Bacille Calmette - Guérin
CBO	Community Based Organisation
CHW	Community Health Worker
COPD	Chronic obstructive pulmonary disease
CPT	Cotrimoxazole preventive therapy
DOH	Department of Health
DOT	Directly-Observed Treatment
DOTS	Directly-Observed Treatment, Short course
DST	Drug susceptibility testing
E	Ethambutol
ETR	Electronic TB Register
GXP	GeneXpert machine
H	Isoniazid
HCW	Health Care Workers
HIV	Human Immunodeficiency Virus
HR	Isoniazid/ Rifampicin
IPT	Isoniazid preventive therapy
LED	Light emitting diode microscope
LPA	Line probe assay (Genotype MTBDR®)
MDG	Millennium Development Goals
MDR-TB	Multidrug-Resistant Tuberculosis
MGIT	Mycobacterial growth indicator tube
NGO	Non-Governmental Organisation
NNRTI	Non nucleoside reverse transcriptase inhibitors
NTM	Non tuberculous mycobacteria
NTP	National Tuberculosis Control Programme
PCR	Polymerase chain reaction
PHC	Primary Health Care
PI	Protease inhibitor
PICT	Provider Initiated Counselling and Testing
PMTCT	Prevention of Mother-to-Child HIV Transmission
PN	Professional Nurse
QA	Quality Assurance
R	Rifampicin
RSA	Republic of South Africa
S	Streptomycin
HRZE	Isoniazid/ Rifampicin/ Pyrazinamide/ Ethambutol
STI	Sexually Transmitted Infections
TB	Tuberculosis
TST	Tuberculin skin test
VCT	Voluntary Counselling and Testing
WHO	World Health Organisation
XDR-TB	Extensively drug-resistant TB
Xpert	Xpert MTB/RIF® Test
Z	Pyrazinamide

DEFINITIONS

Contact	Any person who has been exposed to an index patient
Household contact	A person who shared the same enclosed living space for at least eight continuous hours or for frequent prolonged periods with the index case during the 3 months before commencement of the current treatment episode
Index patient	The first patient to be diagnosed with new or recurrent TB in a specific household or other comparable setting in which others may have been exposed, irrespective of age.
Laboratory turnaround time (TAT)	The time taken from receipt of the specimen in the laboratory to results being dispatched from the laboratory to the facility.
Relapse	Reactivation of latent TB
Re-infection	Newly acquired infection. May be drug-sensitive or drug resistant (primary resistance)
Sputum result turnaround time (TAT)	Time taken from sputum specimen collection to receiving the results back in the facility.
Time to treatment initiation	The time taken from specimen collection to starting the patient on treatment

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1. TRANSMISSION AND PATHOGENESIS OF TB

1.1 Transmission of tuberculosis

There are five closely related mycobacteria responsible for tuberculosis: *Mycobacterium. tuberculosis, Mycobacterium bovis, Mycobacterium africanum, Mycobacterium microti and Mycobacterium. canetti. M. tuberculosis*, by far the commonest, is transmitted between humans through the airborne route. There are no known animal reservoirs of *M. tuberculosis*. *M. bovis* may penetrate the gastrointestinal mucosa or invade the lymphatic tissue of the oropharynx when ingested in milk from diseased cows. Human infection with *M. bovis* has decreased significantly in developed countries as a result of the pasteurisation of milk and effective tuberculosis control amongst cattle. Infection with the other organisms is relatively rare.

Tuberculosis is usually spread from person-to-person through the air by droplet nuclei (<5 microns) that are produced when a person with pulmonary or laryngeal tuberculosis coughs, sneezes, talks or sings. Droplet nuclei may also be produced by aerosol-producing investigations such as sputum induction, bronchoscopy and through manipulation of lesions or processing of tissue or secretions in the laboratory.

Droplet nuclei, which are small particles 1 to 5 µm in diameter containing 1-5 bacilli, are highly infectious. They are so small that air currents normally present in any indoor space can keep them airborne for up to 4 hours. These droplets are small enough to reach the alveolar spaces within the lungs, where the organisms replicate.

Three factors determine the likelihood of transmission of *M. tuberculosis*:

- The number of organisms expelled into the air
- The concentration of organisms in the air, determined by the volume of the space and its ventilation
- The length of time an exposed person breathes the contaminated air

One cough can produce 3,000 droplet nuclei and a sneeze up to a million droplet nuclei; the infectious dose of tuberculosis is 1 to 10 bacilli. The most infectious cases are those with smear positive pulmonary TB, with 3+++ on smear microscopy being the most infectious than 1+. Smear negative pulmonary TB cases are much less infectious. Extra-pulmonary cases are almost never infectious, unless they have pulmonary tuberculosis as well. Individuals with latent tuberculosis infection are not infectious, as they do not have replicating bacteria and cannot transmit the organism.

Transmission generally occurs indoors, in dark, poorly ventilated spaces where droplet nuclei stay airborne for a long time. Direct sunlight quickly kills tubercle bacilli, but they can survive in the dark for several hours. Close contact and prolonged exposure increases the risk of transmission. 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 and only 10% will develop active disease (half of these now and half later on in life). The risk is highest in the first two years after infection, when half the cases will occur. Those most at risk include children <5 years of age and the elderly.

People with suppressed immunity are more likely to develop active TB than those with normal immunity; 50-60% of HIV positive people infected with TB will go on to develop active disease. The annual risk of TB in an HIV positive person is 10% compared to a lifetime risk of 10% in a healthy individual. Immunosuppressive conditions such as silicosis, diabetes mellitus, and prolonged use of corticosteroids and other immunosuppressive drugs are used; also increase the risk of progression to active TB.

In children, malnutrition, measles, whooping cough increase the risk of progression to active TB disease. BCG immunisation gives variable protection against the progression of TB from infection to disease. The main benefit of BCG is the protection against the development of the serious forms of TB in children, such as TB meningitis and disseminated TB.

1.2 Pathogenesis of tuberculosis

After inhalation, the droplet nuclei are carried down the trachea-bronchial tree and deposited in a respiratory bronchiole or alveolus where they are ingested by alveolar macrophages that produce a non-specific response to the bacillus. Infection depends both on the bacterial virulence and the inherent microbicidal ability of the alveolar macrophage that ingests it. If the bacillus is able to survive initial defences, it can multiply within the alveolar macrophage.

The tubercle bacillus grows slowly, dividing approximately every 25 to 32 hours within the macrophage. The mycobacterium has no known endotoxins or exotoxins, so there is no immediate host response to the infection. The organisms grow for 2 - 12 weeks and reach 10^3 to 10^4 in number, which is sufficient to elicit a cellular immune response that can be detected by a reaction to the tuberculin skin test. The destruction of macrophages and release of tubercle bacilli products and chemokines stimulates an immune response.

Before the development of cellular immunity, tubercle bacilli spread via the lymphatics to the hilar lymph nodes and from there through the bloodstream to more distant sites. Certain organs and tissues are notably resistant to multiplication of these bacilli. The bone marrow, liver and spleen are almost always seeded with mycobacteria, but uncontrolled multiplication of the bacteria in these sites is unusual. Organisms deposited in the upper lung zones, kidneys, bones and brain find environments that favour their growth. Numerous bacterial divisions may occur before specific cellular immunity develops, limiting multiplication.

1.3 Primary infection

Primary infection occurs on first exposure to tubercle bacilli. This usually occurs in childhood so primary TB is often thought of as childhood TB. However, it can occur at any age in a previously unexposed individual. Inhaled droplet nuclei containing bacilli lodge in the terminal alveoli of the lungs, usually in the lower part of the upper lobe or upper part of the lower lobe. The bacilli are phagocytosed by the alveolar macrophages; mycobacterial products inhibit the bactericidal activities of the alveolar macrophages, allowing the bacilli to replicate within the macrophages. Other macrophages and monocytes are attracted to the area and produce an immune response. This inflammatory area is known as the Ghon focus.

Bacilli and antigens drain from the Ghon focus via the lymphatics to the hilar lymph nodes and together these form the primary (Ghon) complex. The inflammatory response produces the typical picture of caseous necrosis. Within the lymph node, the T-lymphocytes mount a specific immune response and activated macrophages inhibit the growth of the phagocytosed bacilli. This primary focus contains 1,000–10,000 bacilli that gradually lose their viability and multiply more and more slowly. The inflammatory area in the primary focus is replaced by fibrous scar tissue, sometimes with calcification, in which the macrophages containing bacilli are isolated and die. Some dormant bacilli in the primary focus can survive for months or years: these are known as “latent bacilli”.

Primary infection is usually asymptomatic and a positive tuberculin skin test 4-6 weeks after infection is the only evidence of infection. In a few cases, the immune response is not strong enough to prevent multiplication of bacilli and bacilli may spread from the lymphatics into the bloodstream and throughout the body causing disease within a few months. Primary progressive TB in the lungs leads to enlargement of the primary focus with spread throughout the airways or lymphatics. Multiple areas of caseation and cavitation are found, producing a clinical picture similar to post-primary TB.

Table 1: Possible Outcomes of Primary Infection

NO CLINICAL DISEASE Positive tuberculin skin test (Usual "outcome" in 90% of cases)	**HYPERSENSITIVITY REACTIONS** e.g. erythema nodosum phlyctenular conjunctivitis dactylitis
PULMONARY AND PLEURAL COMPLICATIONS e.g. tuberculous pneumonia lobar collapse (bronchial compression) pleural effusion	**DISSEMINATED DISEASE** e.g. lymphadenopathy (usually cervical) meningitis pericarditis miliary disease

1.4 Post-primary TB / Secondary TB

Post-primary TB is the pattern of disease that occurs in a previously sensitised host. It occurs after a latent period of months or years after primary infection. It may occur either by reactivation of latent bacilli or by re-infection.

Reactivation occurs when dormant bacilli, persisting in tissues for months or years after primary infection, start to multiply. This may be in response to a trigger such as weakening of the immune system by HIV infection. Re-infection occurs when a person who previously had a primary infection is exposed to an infectious contact. In a small number of cases it occurs as a progression of primary infection. Following primary infection, rapid progression to intra-thoracic disease is more common in children than in adults. Chest X-rays may show intra-thoracic lymphadenopathy and lung infiltrates. Post-primary TB usually affects the lungs but can involve any part of the body. The characteristic features of post-primary PTB include upper lobe involvement with cavitation and extensive lung destruction. Sputum smears are usually positive and there is usually no intrathoracic lymphadenopathy.

Pulmonary tuberculosis is the infectious and most common form of TB disease, occurring in over 80% of cases. Laryngeal tuberculosis, although uncommon is also very infectious. Tuberculosis may, however, affect any part of the body. Extra-pulmonary tuberculosis is a result of the spread of mycobacteria to other organs, most commonly pleura, lymph nodes, spine, joints, genito-urinary tract, nervous system or abdomen.

1.5 TB and 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. HIV is responsible for a large increase in the proportion of patients with smear-negative pulmonary and extrapulmonary TB. These patients have inferior treatment outcomes, including excessive early mortality, compared with HIV-positive, smear-positive pulmonary TB patients due to late presentation, diagnosis and initiation of treatment. Therefore rapid diagnoses of not only smear positive PTB but smear-negative pulmonary and extrapulmonary TB and early initiation of treatment is key to reduction of TB mortality in people living with HIV.

HIV infection suppresses the body's immune system by reducing the number of CD4-T cells. This in turn results in the loss of the body's ability to prevent the spread of the tubercle bacilli from localized granulomas resulting in disseminated disease. Rapid progression from initial infection to TB disease may also occur in markedly immunosuppressed patients. TB disease can result in the reduction of the CD4 cells and increase in viral load therefore accelerating the progression of HIV infection to AIDS. Patients with active TB who are HIV-positive have a higher risk of dying from TB than those without HIV.

1.6 TB and Diabetes

The prevalence of TB disease is higher in patients with diabetes compared to those without diabetes mellitus and DM prevalence is high amongst people with TB disease . The relative risk of death among TB patients with Diabetes mellitus is high compared to non diabetic TB patients . The weak immune system associated with diabetes triples the risk of developing among people with diabetes than in the general population. Diabetes is also complicated by the presence of infectious diseases, including TB. Optimizing diabetes management during TB treatment should therefore be a high priority in TB patients in order to improve the general health status of the patient. The regular interaction with health care workers during TB treatment provides an excellent opportunity for health education and counseling for better diabetes control.

1.7 TB and smoking

Passive and active exposure to tobacco smoke is significantly associated with TB exposure and disease. 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;

- impaired clearance of mucosal secretions in the tracheo bronchial tree. This allows the M TB to reach the alveoli.
- impaired functioning of the pulmonary alveolar macrophages, resulting in lower levels of cytokines being secreted.
- decreased intracellular tumor necrosis factor-α production leading to impaired intracellular killing of M TB.

1.8 TB and alcohol

High alcohol consumption (on average >40g alcohol per day) 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 a number of studies have found higher relapse rate among heavy drinkers and those with alcohol use-related health disorders

1.9 TB and silicosis

Silicosis is an occupational lung disease caused by inhalation of silicon dioxide in crystalline forms such as quartz, cristobalite or tridymite. Workers at greatest risk are those that blast rock and sand such as miners, quarry workers and stone cutters. There are three forms of silicosis - classic/ chronic, accelerated and acute. Silica dust is a risk factor for the development of pulmonary tuberculosis. Silica impairs the alveolar macrophages thus weakening the lung's defence mechanisms against MTB. The bacilli can remain encapsulated within the silicotic nodules and can cause reactivation of tuberculosis in patients with silicosis.

2. CLINICAL PRESENTATION OF TB

TB diagnosis depends on symptom screening of all patients (including HIV positive patients) presenting to the health facility and contacts of people with laboratory confirmed pulmonary TB disease. All those who have symptoms of TB disease must be investigated for TB.

2.1 Pulmonary TB

1) Symptoms

The main symptoms of pulmonary tuberculosis are:

- Persistent coughof 2 weeks or more or any duration if HIV positive
- Fever for more than 2 weeks
- Drenching night sweats
- Unexplained weight loss (more than 1.5 kg in a month)

A productive cough, 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.

Some patients may present with chest pains (due to pleurisy, muscle strain), breathlessness (due to extensive lung disease or concomitant pleural effusion), localised wheeze due to local tuberculous bronchitis, or because of external pressure on the bronchus by an enlarged lymph node.

2) Physical signs

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 degrees Celsius)

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.

All individuals suspected of having pulmonary tuberculosis should have at least one sputum specimen examined for bacteriological confirmation of TB disease using the rapid diagnostic tests.

2.2 Extra-pulmonary TB

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

Disseminated tuberculosis and tuberculosis meningitis are acute, severe forms of TB, often occurring soon after primary infection. They occur most commonly in children and young adults. These acute forms of TB are often fatal. When this form of disease is suspected, treatment should be commenced immediately without waiting for bacteriological proof of diagnosis. HIV positive patients particularly those with low CD4 counts may present with extra pulmonary disease. The presentation of extra-pulmonary TB is generally no different between HIV positive and HIV-negative patients, however, differences do occur.

Appropriate investigations for extra-pulmonary TB include the following where these are available (usually only secondary or tertiary hospitals)

- Ultrasound examination may be suggestive of abdominal TB (lymphadenopathy, ascites and/or splenic hypodensities) or pericardial TB (pericardial effusion especially if there is stranding)
- TB blood culture
- Culture of tissue or fluid from fine needle aspirate or biopsy
- Histological examination of tissue
- Cytological examination

1) *TB meningitis*

Before the advent of effective anti-tuberculosis chemotherapy, TB meningitis was uniformly fatal. TB meningitis remains a potentially devastating disease that is associated with a high morbidity and mortality. HIV positive patients appear to be at increased risk for developing TB meningitis but the clinical features and outcome of the disease are similar to that in HIV-negative patients.

Clinical presentation and management;

- Patients present with gradual onset of headache, malaise, confusion, decreased consciousness and sometimes vomiting.
- Examination reveals neck stiffness and a positive Kernig's sign (flex one of the patient's legs at hip and knee with the patient lying on back, and then straighten the knee; resistance to straightening the knee and pain in the low back and posterior thigh suggest meningeal inflammation).
- Diagnosis rests on clinical presentation and a lumbar puncture with examination of cerebrospinal fluid (CSF). The following CSF features are highly suggestive of TB meningitis:
  - Clear CSF
  - Elevated pressure
  - High levels of protein (>1g/ l)
  - High lymphocyte count (30-300/mm^3)
  - Low glucose
  - Negative India ink stain for cryptococcus
  - Negative cryptococcal Antigen test
- Patients with suspected TB meningitis should be referred to hospital without delay as TB meningitis is life threatening, with serious complications if not treated promptly.
- Those presenting with more severe neurological impairment such as drowsiness or coma have a

greater risk of neurological sequelae and a higher mortality.

Table 2.1: CSF Differential Diagnosis for TB Meningitis

Disease	White Cell count	Protein	Glucose	Microscopy
Tuberculous meningitis	Elevated L > PMN	Increased	Decreased	Presence of AFB (rare) MTB may be detected on Xpert
Bacterial meningitis	Elevated PMN > L (L increases with partial treatment)	Increased	Decreased	Presence of bacteria after gram staining
Viral meningitis	Elevated L > PMN	Moderately increased	Normal	Negative
Cryptococcal meningitis	Elevated L > PMN	Increased	Decreased	Presence of yeast shown by India ink stain
L-lymphocytes		PMN-polymorphonuclear leucocytes		

2) Disseminated / Miliary TB

Disseminated TB results from widespread blood borne dissemination of TB bacilli. This is either the consequence of a recent primary infection or the erosion of a tuberculous lesion into a blood vessel. It occurs most often in children and young adults. Unlike pulmonary tuberculosis, acute disseminated TB is highly fatal. Disseminated TB is an under-diagnosed cause of end-stage wasting in HIV positive individuals and should be considered in all febrile patients presenting with HIV wasting syndrome.

When disseminated TB is suspected, treatment should be commenced immediately without waiting for bacteriological proof of diagnosis.

Clinical features

1) The patient presents with a general deterioration in health and constitutional symptoms such as high fever, night sweats, weight loss and shortness of breath.
2) Clinical signs may reflect the involvement of other organs: pleural effusion, digestive problems, hepatosplenomegaly and meningeal signs.
3) There may be choroidal tubercles on fundoscopy.
4) Other conditions that may present in a similar way and need to be excluded, include: acute viral infections, as well as infections caused by staphylococcus aureus, salmonella species, cryptococcus and malaria.

Diagnosis

1) Chest X-ray may show diffuse, uniformly distributed, small miliary ("like small millet seeds") nodules.
2) Full blood count may show pancytopenia (this may also be seen as a result of HIV) or anaemia.
3) Liver function tests may be abnormal.
4) Bacteriological confirmation is sometimes possible from sputum, C.S.F., or bone marrow.
5) Smear microscopy of sputum from cases with disseminated (miliary) tuberculosis is usually negative, as the disease is paucibacillary.

3) Tuberculous lymphadenopathy

TB lymphadenopathy, caused by lymphatic spread of the organism, is one of the commonest forms of extra-pulmonary TB. Involvement of the lymph nodes is usually a complication of primary TB and is commoner in children. It is to also found in the later stages of HIV infection.

Clinical features

- Large mediastinal lymph nodes can compress the airways leading to an audible wheeze or typical brassy cough.
- Peripheral TB lymphadenopathy most commonly occurs in the neck and armpits. Typically lymph

nodes are large (>2 cm), tender, non-symmetrical, matted, firm to fluctuant and rapidly growing.

- Associated systemic features include fever, night sweats and weight loss.
- As nodes increase in size and become fluctuant, they may suppurate and drain via a chronic fistula, resulting ultimately in scarring.
- TB lymphadenopathy needs to be differentiated from persistent generalized lymphadenopathy (PGL). PGL develops in up to 80% of HIV-infected individuals during the early stages of infection. These lymph nodes are typically non-tender, <2 cm in size and symmetrical. PGL requires no treatment.
- TB infected lymph nodes decrease extremely slowly in size (over weeks or months) on treatment, and in a few cases, are still the same size after the treatment has finished. This does not mean that the treatment was not successful.

Diagnosis

- If a lymph node is exuding caseous material through a fistula, this can sent to the laboratory for TB investigations.
- Otherwise, the patient may be referred to a doctor/ hospital for conduct a fine needle aspirate of the lymph node to be conducted. This should be sent for Xpert MTBRIF testing or culture. A lymph node biopsy, which is a more complicated procedure, may be conducted.
- Chest x-rays may be useful in diagnosing mediastinal TB lymphadenopathy.
- Intra-abdominal lymphadenopathy is more readily detected by ultrasound or computerised axial tomography (CT scan). These cases are treated empirically, unless the nodes can be readily aspirated at a tertiary health facility.

4) Tuberculous serous effusions

Inflammatory tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities. They are a common form of TB in HIV positive patients. In populations with a high prevalence of HIV, TB is the commonest cause of a serous exudate.

Patients usually have systemic and local features. Microscopic examination of the aspirate rarely shows AFBs because the effusion is a result of an inflammatory reaction to TB lesions in the serous membrane. TB culture is of no immediate help because a culture result takes up to six weeks or more. The aspirate is an exudate with a protein content of more than 30g/l. A biochemical test is not required to diagnose an exudate: let the aspirated fluid stand for a while - if it clots, it is an exudate. However, failure of the aspirate to clot does not exclude TB as it may indicate a low protein content, which is found in wasted patients.

a) Tuberculous pleural effusion

Tuberculous pleural effusion is the commonest cause of a unilateral pleural effusion in countries with a high TB burden. It is also the commonest form of HIV-related extra-pulmonary disease, with a mortality of about 20% in the first 2 months on treatment. Management of tuberculous pleural effusion should aim at starting TB treatment promptly and determining the HIV-status of the patient.

Clinical features

- Presentation is most often acute with a non-productive cough, chest pain, shortness of breath and high temperature.
- The chronic form is found predominantly in the elderly and presents with systemic symptoms such as weakness, anorexia, weight loss, slight fever, cough, and chest pain.
- Findings on clinical examination may include:
  - Tracheal and mediastinal shift away from the side of the effusion
  - Decreased chest movement
  - Stony dullness on percussion on the side of the effusion.

Diagnosis

- Suspected pleural effusions should be confirmed immediately by chest x-ray. This will show unilateral, uniform white opacity, often with a concave upper border.
- Pleural aspiration should be undertaken wherever possible: the fluid is a straw coloured exudate and has protein content >30g/l. The white cell count is high (1000-2500 per mm^3) with predominantly lymphocytes. The adenosine deaminase (ADA), which is a measure of the lymphocyte count, is raised >30 IU.
- Failure of the aspirate to clot does not exclude TB as it may indicate lower protein content in wasted patients; the predominance of lymphocytes (>50%) confirms a TB diagnosis.
- Since the number of bacilli present is relatively small, AFB are not usually seen on microscopy of centrifuged specimens of pleural fluid, however, culture may be positive.
- If aspiration is not possible, commence TB treatment unless the chest x-ray suggests a different diagnosis.
- Differential diagnosis of a pleural exudate includes malignancy, a post-pneumonia effusion and pulmonary embolism.
- Bilateral effusions or those with cloudy or bloody aspirates should be investigated further.
- Xpert MTBRIF may be requested on pleural biopsies to confirm

b) Tuberculous pericardial effusion

Tuberculosis accounts for about 90% of pericardial effusions in HIV positive patients and for about half in HIV-negative patients.

Clinical features

- Cardiovascular symptoms include: chest pain, shortness of breath, cough, dizziness and weakness due to low cardiac output.
- Symptoms of right-sided heart failure include leg swelling, right hypochondrial pain (liver congestion), abdominal swelling (ascites).
- Signs include: tachycardia, low blood pressure, pulsus paradoxus (fall in systolic pressure >10mHg on inspiration), raised jugular venous pressure, impalpable apex beat, distant heart sounds and a pericardial friction rub.
- Signs of right-sided heart failure include hepatosplenomegaly, ascites, and peripheral oedema.

Diagnosis

Diagnosis usually rests on suggestive systemic features and ultrasound:

- Chest X-ray may show a large globular heart, clear lung fields and bilateral pleural effusions.
- ECG may show tachycardia, flattening of ST and T waves, low voltage QRS complexes.
- In cases of cardiac tamponade the patient should be referred to a specialist for aspiration of the effusion.
- Treatment without pericardiocentesis usually results in resolution of a tuberculous pericardial effusion.

In high TB and HIV prevalent populations, TB is the most likely treatable cause of a pericardial effusion. It may be safer for the patient to start empiric TB treatment than to undergo diagnostic pericardiocentesis. Treatment is the same as for all types of TB, but corticosteroids may be added. If not properly treated, TB pericarditis may evolve to constrictive pericarditis over months, with later evidence of calcification.

c) Peritoneal Tuberculosis

Peritoneal TB is the commonest type of abdominal TB.

Clinical features

- Clinical features include systemic features and ascites with no signs of portal hypertension.
- There may be palpable abdominal masses (mesenteric lymph nodes).
- Bowel obstruction may develop from adhesion of caseous nodules to bowel.

Diagnosis

- Always do a diagnostic ascitic tap - the aspirated fluid is usually straw coloured, but is occasionally turbid or blood stained. The fluid is an exudate, usually with more than 300 white cells per mm^3 with lymphocytes predominating (in spontaneous bacterial peritonitis which is a common complication of cirrhosis, polymorphonuclear leucocytes predominate).
- Investigate for pulmonary TB
- Abdominal ultrasound may show retroperitoneal or mesenteric lymph node enlargement
- Diagnosis is usually presumptive - in doubtful cases, a macroscopic examination and bacteriological or histological examination of the samples may be considered in a hospital where exploratory surgery or laparoscopy can be performed.

d) Tuberculous empyema

- This usually arises when a tuberculous cavity in the lung ruptures into the pleural space.
- The physical signs are similar to a pleural effusion, but aspiration reveals thick pus. Send the pus to the laboratory for examination for TB, gram stain and bacterial culture. The main differential diagnosis is bacterial empyema.
- A succussion splash is a splashing sound heard with the stethoscope while shaking the patient's chest. It indicates a pyopneumothorax (pus and air in the pleural space). After chest x-ray confirmation of a pyopneumothorax, insert a chest drain with underwater seal to remove fluid and air.

5) Tuberculosis of the spine

TB can affect any bone but most commonly affects the vertebral column. It is seen both in children and adults and can be severe, with neurological sequelae. Involvement of the intervertebral disc occurs by spread of a lesion from the vertebral body. In many cases more than one intervertebral disc is involved. It is characterised by loss of bone density and slow bone erosion, with the disc space being maintained for a long time (differentiating it from pyogenic infections). In children, an acute form may develop with vertebral osteomyelitis, collapse of the vertebral body and neurological involvement. Collapse of adjacent vertebral bodies may lead to angulated kyphosis. Thrombosis of the anterior spinal artery caused by the inflammation causes transverse myelitis and paralysis.

Spread may occur into the soft paravertebral tissue to form a so-called "cold abscess". These form symmetrical masses; they may spread further and end up calcifying.

Clinical features

- Features include back pain, stiff back, reluctance to bend the back
- There may be referred pain radiating out from the site of origin
- Localised swelling, sometimes with an obvious lump or abnormal curvature of the spine
- A child that refuses to walk or has weakness or paralysis of the lower limbs.
- Involvement of cervical vertebrae may cause pain in the neck and shoulders and rigidity of the neck. A cold abscess can develop behind the sternocleidomastoid muscle. More rarely, neurological involvement leads to progressive tetraplegia.
- Involvement of the thoracic vertebrae causes localized back pain, deformity of the spine, and in extreme cases an angulated kyphosis (gibbus). The chief risk is spinal cord compression and paraplegia.
- Involvement of the lumbar vertebrae results in lower back pain. A "cold abscess" from here can drain along the psoas muscle towards the inguinal area.
- In the early stages the physical examination can be non-specific.
- Patients with weakness or paraplegia should be referred to a specialist urgently.

Diagnosis

- X-rays of the spine show disc space narrowing and erosion of the adjacent vertebral bodies, wedge shaped collapse and angulation.
- Biopsy of cold abscess for microscopy and culture if possible, can confirm the diagnosis.
- Differential diagnosis includes degenerative disc disease, infectious spondylitis and cancerous vertebral metastases.

2.3 Diagnosis of TB in HIV positive patients

Tuberculosis can occur at any point in the course of HIV infection. Pulmonary tuberculosis is the most common manifestation of tuberculosis in adults infected with HIV. The clinical pattern of tuberculosis correlates with the patient's immune status:

- In the early stages of HIV infection when immunity is only partially compromised, the features are more typical of post-primary TB.
- As immune deficiency worsens, HIV-infected patients present with atypical pulmonary disease resembling primary TB or with extra-pulmonary TB or disseminated disease.

Table 2.2: Clinical picture, sputum smear and chest x-ray appearance in HIV infection

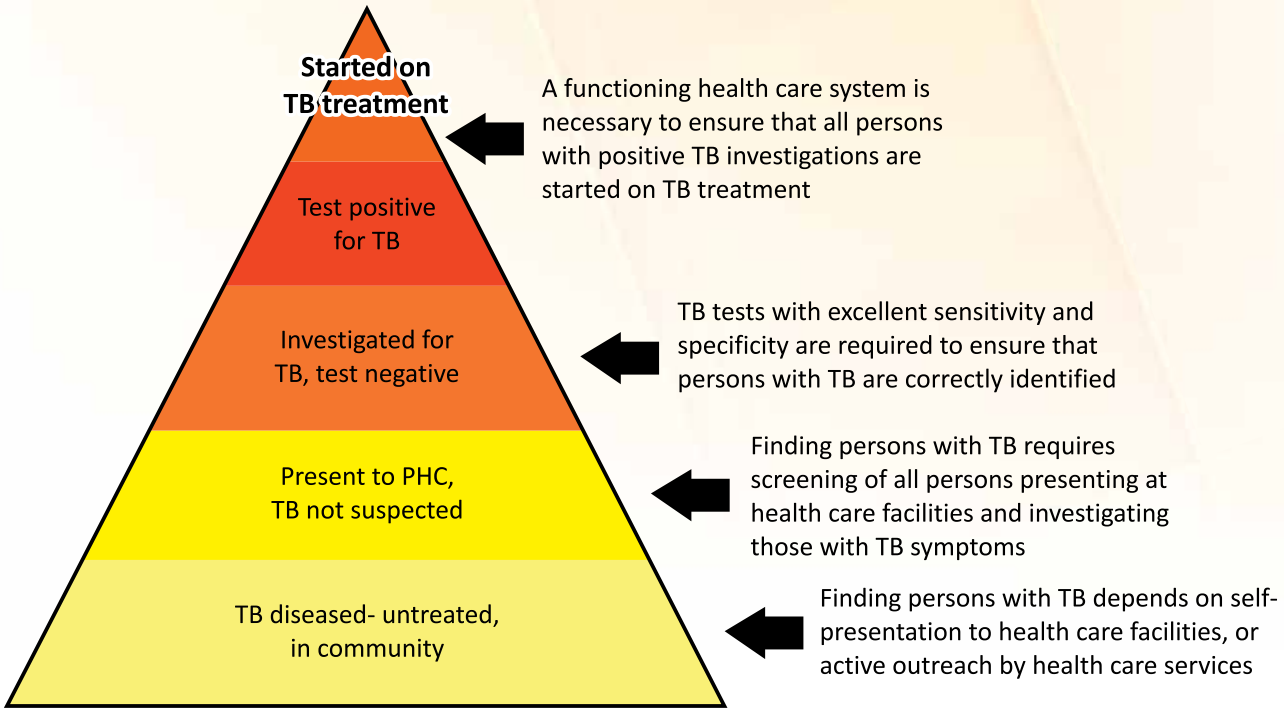
	Early HIV Infection	Late HIV Infection
Clinical picture	Resembles TB in HIV-uninfected person	Often extrapulmonary or disseminated, more rapid disease progression
Sputum smear results	Usually positive	Often negative
Chest X-ray appearance	Often cavities	Hilar lymphadenopathy, infiltrates, no cavities. Can be normal.

Unlike many other infections that develop only when the CD4 counts falls below 200/mm^3, the risk of TB is increased even in the first year of HIV infection. This means that TB is one of the earlier infections to occur in an HIV positive patient; it may therefore happen that TB is diagnosed before HIV in co-infected patients.

3. DIAGNOSIS OF TUBERCULOSIS

The diagnosis of TB depends on numerous factors namely; self-presentation of persons with TB symptoms to health care facility, high index of TB suspicion among health care professionals, TB screening practices in health facilities, sensitivity and specificity of diagnostic test used, turnaround time for delivery of laboratory results, and the capacity to trace people with positive results and start them on treatment. This is summarised in the figure below.

Figure 1: Steps required for the diagnosis of TB.



Traditionally, TB services have relied on passive, self presentation of persons with TB symptoms to the health care facilities. Increasing community awareness of TB symptoms will cause more persons with TB symptoms to present earlier to a health care facility for investigation for TB. It is also possible to look for persons with TB through active, community or facility based interventions such as community outreach events to schools, places of work, or through screening or investigating persons who have had contact with someone with recently diagnosed TB. The aim is to screen every person for TB annually.

3.1 Diagnostic tests for TB

The table below presents a summary of the available tests for bacteriological confirmation of TB

Test	Type available	Strengths	Weaknesses
Microscopy	LED/ Fluorescent microscopy	High specify Short TAT	Low sensitivity in people with low bacillary load i.e. children and PLWHA
Culture	Liquid (MGITT) Solid	High sensitivity	Long TAT High contamination rates (liquid culture)
PCR based assays	Line Probe Assay	Short TAT Detects Rif and INH resistance High sensitivity for MDR-TB	Reduced sensitivity in smear negative
	Xpert MTB/RIF	Short TAT Detects Rif resistance High sensitivity for Rif resistance	Does not detect INH resistance Reduced sensitivity in smear negative

3.1.1 Smear microscopy

The diagnosis of TB historically relied on the identification of acid fast bacilli through microscopic examination of stained sputum smears. Smears may be prepared directly from clinical specimens or from concentrated preparations. Two staining methods can be used to observe acid-fast bacilli: Ziel-Neelsen staining or fluorescent auramine staining. The staining procedure depends on the ability of mycobacteria to retain these dyes when treated with acid and alcohol solutions. Eighty percent of smear results should be available within 48 hours.

Smear microscopy has good specificity for TB but has very low sensitivity in detecting TB in patients with non cavitary pulmonary disease or low bacillary load in sputum (e.g. HIV positive patients).

The number of bacilli (AFB) seen in a smear reflects the patient's infectivity. The laboratory records the number of bacilli seen on each smear as follows:

ZN Staining		Auramine Staining	
Number of bacilli seen on smear	**Results reported**	**Number of bacilli seen on smear**	**Results reported**
No AFB per 100 oil immersion field	0	No AFB on slide	0
1-9 AFB per 100 oil immersion field	Scanty	<1 AFB per field	+
10-99 AFB per 100 oil immersion field	+	1-9 AFB per field	++
1-10 AFB per 1 oil immersion field (min 50 fields)	++	10-99 AFB per field	+++
>10 AFB per 1 oil immersion field (min 20 fields)	+++	>100 AFB per field	++++

The results of laboratory reports are subject to various sources of error including: poor quality of specimens, clerical errors, handling errors, process errors and poor quality control. A laboratory result that does not tie up with other clinical information must be interpreted with care.

3.1.2 Culture methods

Culture is more sensitive than smear microscopy, detecting a higher proportion of cases among patients with symptoms. Further identification is performed on positive cultures to distinguish TB from NTMs. However, it is an expensive and slow diagnostic technique, not accessible to some patients. Time to positive results depends on bacilliary load and should be positive by 4 weeks in most cases; however a culture is only reported as negative at the end of 6 weeks incubation. Culture is however an important diagnostic tool in patients with paucibacillary tuberculosis, such as HIV positive patients with smear-negative pulmonary tuberculosis and children.

Indications for sputum culture include:

- To diagnose paucibacillary disease in TB suspects (e.g. HIV positive patients) who have two negative smears.
- For drug susceptibility testing in TB suspects with a history of previous TB treatment (interruption, failure, relapse) patients who remain smear positive at the end of the intensive/ continuation phase of treatment or who fail to improve clinically during treatment.
- For drug susceptibility testing in people at high-risk of DR-TB such as MDR and XDR-TB contacts, health care personnel and prisoners.

Where GeneXpert is available, culture may still be required for:

- HIV positive TB suspects who have a negative GeneXpert test
- TB cases diagnosed as Rifampicin resistant on GeneXpert for susceptibility testing of other drugs
- In unusual cases where despite a Rifampicin susceptible result the patient is failing treatment and treatment adherence is good and thus resistance to drugs other than Rifampicin is suspected.

Traditional culture uses a solid medium such as coagulated egg (e.g. Löwenstein-Jensen) or agar (e.g. Middlebrook 7H10) as a base. Solid media are simple and cost effective to use. Disadvantages include slow bacterial growth (3-4 weeks) and errors due to manual reading of results. The development of more sensitive liquid medium culture techniques, has allowed for the more rapid detection of TB bacilli, within 7 to 14 days. Automated systems are used to culture mycobacteria in liquid media. These systems use specialised vials/ tubes which are inoculated with the patients specimens. Liquid culture is more prone to contamination than solid culture.

Several mechanisms are used to detect the growth of mycobacteria. The MGIT 960 system detects bacterial growth using a fluorescence- quenching based oxygen sensor within each tube. As mycobacteria multiply within the tube, oxygen is consumed and fluorescence is detected by the system. A positive culture may be due to growth of TB but also bacteria, fungi and non-tuberculous mycobacteria. Therefore, a tube that flag positive (culture positive result), the growth in the tube must be stained and examined microscopically to detect the presence of mycobacteria and tested for the presence of TB using molecular probe-based assays or TB antigen tests to rapidly confirm the presence of MTB complex.

Smear microscopy requires ~10 000 TB bacilli per ml of sputum to be detected/positive.
Culture can be positive with only ~10 - 100 TB bacilli per ml of sputum
GeneXpert requires ~ 130 TB bacilli per ml of sputum for a positive result

3.1.3 Drug susceptibility testing (DST)

The Agar proportion method uses the inoculation of drug free and drug containing solid media with the same quantities of a homogenous suspension of cells. The ratio of the colony forming units in both media determines whether the isolate is susceptible or resistant to the drugs tested. This method is the traditional method for DST. The commonly used method is the broth based DST, using either the BACTEC 460 or the MGIT960 system. The drug free and drug containing tubes are inoculated with the homogenous suspension of cells and incubated. The fluorescence of the drug containing tube is the compared with the control which is the drug free tube.

The phenotypic DST methods use critical concentrations for each TB drug. An isolate is considered to

be resistant to a drug when growth in the presence of a critical drug concentration exceeds growth of the same isolate diluted 1:100 in drug-free media. DST for isoniazid should be performed using two critical concentrations: low and high level. Isolates resistant to the low-level critical concentration but susceptible to the high-level critical concentration should be reported as having low level resistance to isoniazid. These patients will benefit from higher dosage of isoniazid in their treatment.

Phenotypic DSTs require a positive culture (4-6 weeks) before testing for drug susceptibility can be performed. This takes an additional 2-3 weeks. Phenotypic DSTs can be performed for the following drugs: Rifampicin, Isoniazid (high and low), Ethambutol, Pyrazinamide, Streptomycin, Amikacin, Kanamycin, Capreomycin, Ethionamide, Ofloxacin, Moxifloxacin.

The Agar proportion method is performed by inoculating drug free and drug containing solid media with the same quantities of a homogenous suspension of MTB bacteria. The ratio of the colony forming units in the two media determines whether the isolate is susceptible or resistant to the drugs tested. This method is the traditional method for DST.

The commonly used method is the broth based DST, using either the BACTEC 460 or the MGIT960 system. The drug free and drug containing tubes are inoculated with a homogenous suspension of MTB bacteria and incubated. The fluorescence of the drug containing tube is then compared with the drug free tube. These patients will benefit from adding isoniazid in their treatment.

3.1.4 Molecular Testing

Note that in South Africa we have 2 different PCR technologies available and provide different information that is helpful in the management of TB. These are;

1. The Gene Xpert (GXP) which is useful for rapidly diagnosing TB and will soon replace microscopy as the 1st line diagnostic test. In addition it allows rapid screen to exclude Rifampicin resistance in most cases.
2. The Line Probe assay is useful for drug resistance confirmation and detects resistance to both Rifampicin and Isoniazid.

3.1.4.1 Xpert® MTB/RIF

The test is called *Xpert MTB/RIF* and the instrument is a GeneXpert (GXP). GeneXpert is an automated molecular platform to detect M. tuberculosis and rifampicin resistance testing by targeting specific mutations in the rpoB gene. It is approved for use directly on raw sputum and results should be available within 2 hours in the laboratory but available in health facilities within 48 hours.

The test involves only three manual steps:

- the addition of sample treatment reagent to liquefy and inactivate the sputum
- the transfer of 2ml of liquefied sputum to the cartridge
- loading the cartridge into the device for the assay.

Advantages of the test are that;

- It detects MTB and Rifampicin resistance from one specimen at the same time.
- Processing time for the test itself is approx. 2 hours.
- It is specific for MTB complex; (it can differentiate MTB from other mycobacteria).
- It can also be used on the following processed samples - CSF, aspirates (gastric, lymph node) and tissue (i.e. pleural biospy)
- The test for each specimen is carried out in a closed system (cartridge), so there is a reduced risk of cross-contamination and human error.

The limitations of this test are that;

- It cannot be used for monitoring treatment because it does not distinguish between live and dead bacilli, its use is therefore limited to diagnosis
- A small proportion of Rifampicin resistance detected may not correlate with physiological resistance (leading to discordance between Xpert and DST results or clinical outcome)
- The assay is semi-quantitative and defines a positive test as “very low”, “low”, “medium”, and “high”. This grading is not reported on the laboratory result. There is no direct correlation between the Xpert semi-quantitative result and the smear grading of scanty, +, ++ and +++.

The rifampicin results can only be reported if MTB complex is detected. If MTB complex is not detected there will be no rifampicin result. Xpert MTB/RIF is a more sensitive test than smear microscopy, therefore it is possible for a TB patient to be Xpert MTB positive but smear negative.

The test might be unsuccessful due to laboratory test errors, test failure or invalid results. In these instances a second specimen must be collected for a repeat Xpert test.

3.1.4.2 Line Probe Assays

These tests have been approved for direct testing on smear positive specimens and on isolates from solid and liquid culture. The test that is available in the country is the Genotype® MTBDRplus assay which is a PCR based hybridisation assay. It simultaneously detects MTB complex and specific mutations in the rpoB gene conferring rifampicin resistance and mutations on the katG gene which is associated with higher levels of isoniazid resistance and inhA gene mutations which is associated with lower levels of isoniazid resistance. Some studies have shown an association between the inhA mutation and ethionamide resistance. These associations can be used as a guide whilst awaiting phenotypic confirmation.

Compared to phenotypic DST this provides rapid diagnosis of drug resistant TB and results should be available within 48 hours in the laboratory and 7 days in health facilities for smear positive TB. For smear negative TB, this depends on the time to positive culture before the LPA can be performed.

Advantages of the test are that;

- It detects MTB and resistance to RIF & INH at the same time from one specimen
- It reduces time to diagnosis of MDR-TB to 7 days
- It is specific for MTB complex; it can differentiate MTB from other mycobacteria.

The limitations of the test are that;

- It cannot be used for monitoring patients on treatment because it does not distinguish between live and dead bacilli, therefore its use is limited to diagnosis
- It is dependent on smear results, can only be performed on smear positive or culture positive sputum specimen
- The test is labour intensive and is prone to contamination and human error
- It requires a lot of space - at least 3 separate rooms for the different steps

A small proportion of resistance detected may not correlate with physiological resistance (leading to discordance between LPA and conventional DST results or clinical outcome). The genetic mechanisms of isoniazid resistance are more complex than rifampicin resistance, thus the test is less sensitive for detecting isoniazid resistance and false susceptible results may occur. Version 2 of the MTBDRplus which can be used on smear positive and negative sputum specimens is available and currently being validated in the country. MTBDRsl is available for second line testing. This test may be used as a rule in test for XDR-TB in high risk groups.

3.2 Other tests that are available

3.2.1 Interferon gamma Release Assays (IGRA)

IGRAs are blood tests that detect MTB infection but cannot distinguish latent TB from active TB. They are not affected by previous BCG vaccination. WHO does not recommend these tests for program purposes in low and middle income settings which includes South Africa. There may be a potential role in specialised settings in screening neonates with exposure to TB as well as patients on TNF – alpha antagonists.

3.2.2 Blood culture

Blood cultures may be used to detect MTB and other species of mycobacteria in HIV-infected patients; especially those with low CD4 count where disseminated disease is suspected. Blood culture bottles specifically designed for the growth of MTB should be used which are different from those used for general investigations. There is no role for blood culture in diagnosing TB at primary health care level, but blood culture may be used at higher levels of care with patients have greater severity of disease.

3.2.3 TB LAM (lateral flow version)

This assay detects lipoarabinomannan (LAM) antigens in urine. LAM is a component of the mycobacterial outer cell wall that is shed from metabolically active or degrading cells and is cleared by the kidney and detectable in urine. It has been reported to have good sensitivity in HIV-infected patients with low CD4 (<50cells/mm^3) cell counts. In a clinical setting this test may have a role in diagnosis if used in combination with other tests to support a diagnosis of TB in patients with advanced immunosuppression. Further studies are required to determine the role of this test in programmatic settings.

3.2.4 Histological examination

Histo-pathological examination may be conducted on tissue specimen, but this is not considered to be bacteriological confirmation of disease. The multiplication of tubercle bacilli in any site of the body causes a specific type of inflammation, with formation of characteristic granuloma that can be found on histo pathological examination. Samples that can be submitted for examination include;

- Fine needle aspiration from lymph nodes
- Tissue biopsies from serous membranes, skin, pleura, endometrium, liver

3.2.5 Tuberculin skin test

The tuberculin test has limited value in clinical work, especially where TB is common. The test shows hypersensitivity to proteins of the TB bacillus, as a result either of infection with M. tuberculosis or induced by Bacille Calmette-Guérin (BCG) vaccination. A positive TST does not indicate TB disease, only infection. Infection is one of the criteria used in the diagnosis of TB in children. A negative result does not rule out the diagnosis of TB disease as various conditions, including HIV, may suppress the reaction.

The WHO has recently reviewed data on the performance of serological tests for TB and has strongly recommended that these tests should NOT be used in the diagnosis of TB infection or disease.

3.3 Adjunctive tests

3.3.1 Chest x-rays

Whilst chest x-rays are quick and convenient, reliance on them as the only diagnostic test results both in over-diagnosis of TB and missed diagnosis of TB. Many diseases mimic TB on chest x-rays and this may lead to an incorrect diagnosis. Chest x-rays may also show lung fibrosis or destruction due to old TB, leading to over diagnosing pulmonary TB.

Chest x-rays are necessary in patients who cannot produce sputum or who have negative Xpert results and are HIV positive, and where extra pulmonary TB (such as pleural effusions and pericardial TB) is suspected. While CXR is non-specific for TB, the presence of infiltrates, lymph nodes or cavities is highly suggestive of TB. The x-ray findings must be interpreted in the light of the patient's history and clinical findings.

Other indications for the use of chest x-rays include;

- To assist in the diagnosis of suspected complications of TB disease such as pneumothorax, pleural effusion or patients with frequent or severe haemoptysis.
- To help in diagnosing other concomitant lung diseases such as lung cancer, bronchiectasis, lung abscess and pneumoconiosis.

3.3.2 Ultrasound

The ultrasound can be used as a supplementary investigation in the diagnosis of extrapulmonary TB particularly abdominal and pericardial TB.

3.3.3 Computerized Tomography (CT scan) and Magnetic Resonance Imaging (MRI)

The use of CT scan and MRI are not widely recommended because they are expensive but they have proved useful for imaging tuberculosis lesions. It provides more detailed images of body parts not easily seen on a standard x-ray. The CT scan may be of diagnostic value in;

- Children and immune compromised people suspected to have TB but without any positive findings
- Patients with normal or inconclusive chest x-ray where TB complications are suspected
- Patients with extra-pulmonary TB

3.3.4 Erythrocyte Sedimentation Rate (ESR)

This test is not a confirmatory test for TB. A number of infections and diseases result in elevated ESR, therefore low specificity for TB.

3.3.5 Adenosine DeAminase (ADA)

ADA is an enzyme found in most cells, it is elevated in TB effusions (>30µl). This test may therefore be useful in confirming the cause of an effusion when it doubt.

3.4 Sputum specimen collection

The detection of MTB is dependent on the quality of the specimen provided. Therefore proper specimen collection and prompt transportation to the laboratory are important in ensuring quality results. If an additional specimen is required this can be collected at least an hour later or preferably in the morning of the following day.

- Sputum collection occurs in a well-ventilated area or outside, but in private and without others watching. The collection must be supervised. The patient must be informed and understand the instructions for sputum collection. The supervisor must not stand in front of the patient.
- Ask the patient to rinse out their mouth with water.
- Advise the patient to be very careful and direct the sputum into the container so as not to contaminate the outside of the container.
- Give the patient the container, without the lid.
- Demonstrate a deep cough from the bottom of the chest, beginning with deep breathing.
- Be ready to replace the lid on the container immediately.
- Once the specimen is in the container, securely close the lid by pressing down on the centre of the lid until a click is heard.
- Wash your hands after handling the sputum specimen.

Table 3.1: Methods of obtaining a sputum sample

Method	Description	Advantage	Disadvantage
Sputum sample	Patient coughs up sputum into sterile container	Easy to perform	• Patient may not be able to cough up sputum • Education and supervision of the patient is required
Nebulisation/ Sputum induction	Patient 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 • May cause bronchospasm
Gastric washing/ aspirate	A tube is inserted into the stomach through the patients mouth or nose to obtain swallowed sputum	Used to obtain sputum in children who do not cough up sputum	• Must be done early morning before eating • Patient 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 diseased 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

Collection of extra pulmonary specimen

Patients suspected to have extra-pulmonary TB should have specimens obtained from the suspected site and Xpert MTBRIF, culture and DST conducted. This is important for the early diagnosis of drug resistant TB particularly in high risk groups.

Xpert MTBRIF may be conducted on gastric washings/ lavages, lymph node fine needle aspirates, cerebrospinal fluid and pleural biopsies.

3.4.1 Completion of the laboratory form

Complete the standard National Health Laboratory Services (NHLS) TB investigation form.

- Name of clinic / hospital details.
- Patient details
- Name and registration number of person requesting the tests
- Date, time and type of specimen collected
- Relevant clinical information on the patient
- Indicate whether this is a new or re-treatment patient
- Indicate whether the specimen is pre-treatment (suspect), follow-up (7 weeks) or end of treatment specimen (23 Weeks).
- Tick the test that is required – where more than one test is requested tick each relevant box. Please indicate test required clearly.
- Indicate clearly under remarks if the sputum specimen was obtained by nebulisation, gastric aspiration, bronchoscopy etc.
- Check the quantity of sputum produced, this should ideally be 5ml or more. If it less, the patient must be requested to cough up more sputum
- Note the appearance of the sputum and ensure that it is sputum and not saliva that is submitted.
- Place the sputum bottle in the plastic bag provided by NHLS to prevent contamination. The laboratory form goes into a separate sleeve in this bag.
- Send the specimen to the laboratory as soon as possible
- Store sputum specimen in a fridge (not a freezer) if transport is not immediately available.

3.4.2 Transportation of sputum specimens

Specimens should be kept in a cold and dark container during transportation, in order to reduce contamination with other non mycobacterium contaminants and enhance the recovery of mycobacteria. The dispatch form must be correctly completed and signed by the designated person in the facility.

The results of laboratory reports are subject to various sources of error including: poor quality of specimens, clerical errors, handling errors, process errors and poor quality control. A laboratory result that does not tie up with other clinical information must be interpreted with care.

3.4.3 Completion of the Case Identification and Follow-Up Register

Record the patients' details and the date on which the specimen was collected in the Case Identification and Follow-Up Register. The register should be updated on a daily basis (with patient's results and treatment commencement dates)

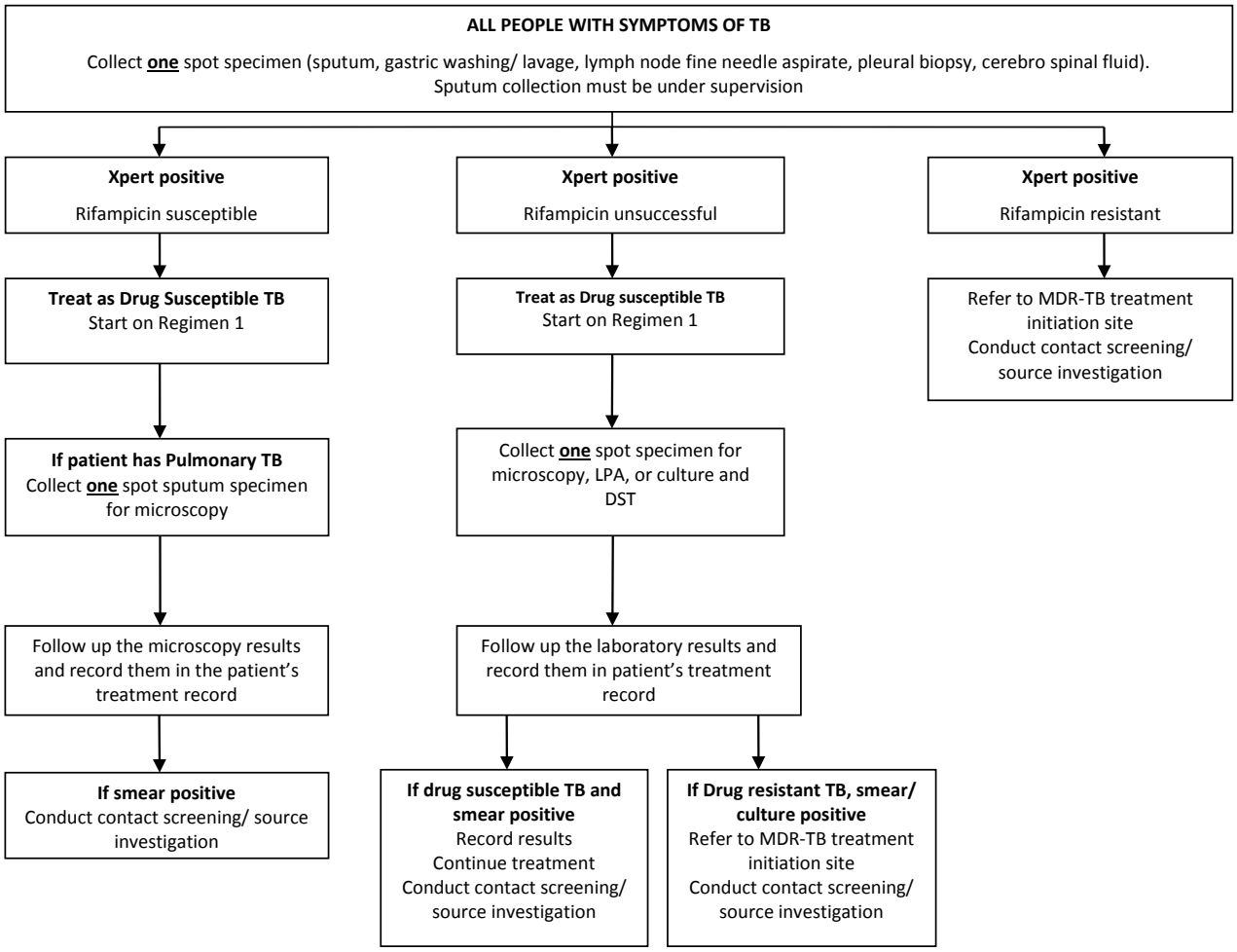
3.4.4 Time to initiation of treatment

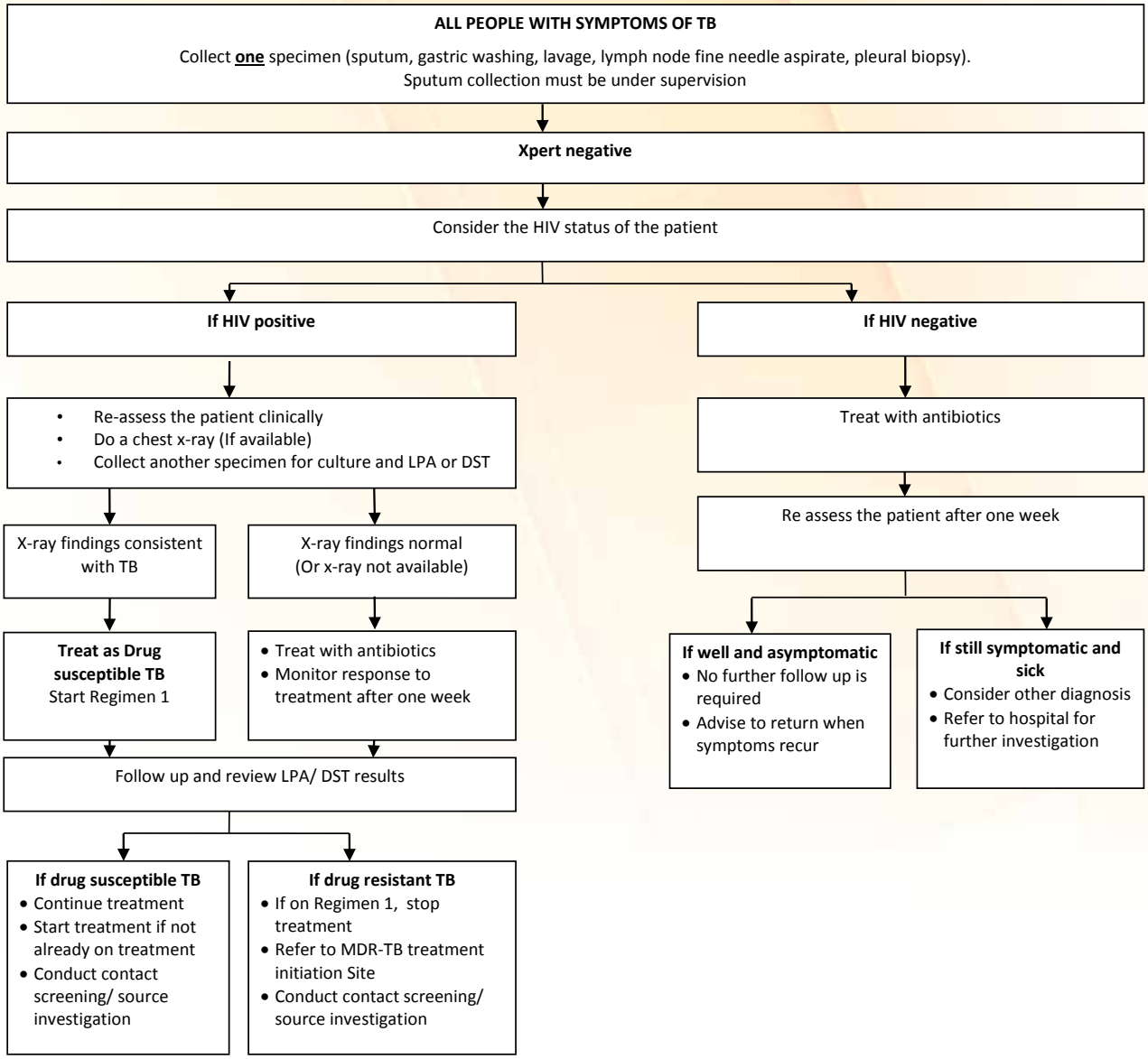
All patients diagnosed with drug susceptible TB must be started on TB treatment within 2 days and those with drug resistant TB within 5 days of suspicion. Laboratory confirmed TB patients who are never started on treatment are referred to as "initial loss to follow up" (Initial defaulters). These patients could have died (but confirmation not available) before initiation of treatment or could not be found on tracing. This measures the efficiency of the TB programme in ensuring that all bacteriologically confirmed patients are started on treatment.

4. TB DIAGNOSTIC ALGORITHMS AND INTERPRETATION

This chapter describes the revised algorithms for TB diagnosis, drug susceptibility testing and management of the patients based on the test results. All individuals who present with symptoms of pulmonary TB should have at least one sputum specimen examined for bacteriological confirmation of TB disease. Rapid tests for confirmation of drug resistant TB such as Xpert or LPA are recommended for early triaging and treatment initiation for patients with DR-TB. Culture and DST will still be used to confirm MDR-TB and resistance to second line drugs, smear microscopy will be used for monitoring progress on treatment.

4.1 XPERT DIAGNOSTIC ALGORITHM





NOTE: *In patients with NTM, MTB will not be detected by Xpert, therefore a culture and speciation or LPA must be conducted*

4.1.1 Interpretation of Xpert results

Note that the GeneXpert provides two results – confirmation of presence of MTB and drug susceptibility testing result.

Result	Meaning	Comment
1. TEST TO CONFIRM PRESENCE OF MTB		
Mycobacterium tuberculosis (MTB) complex detected	MTB was isolated from the specimen therefore the patient has bacteriologically confirmed TB	The patient has TB disease and should be treated
Mycobacterium tuberculosis (MTB) complex not detected	MTB was not isolated from the specimen	This result does not exclude TB in people with paucibacillary disease i.e. children and HIV positive people and EPTB. The sensitivity of Xpert is low in smear negative, culture positive patients. It means that TB disease could not be confirmed bacteriologically Further investigations are required to confirm TB in these patients
2. SCREENING TEST TO RULE OUT RIFAMPICIN RESISTANCE		
Rifampicin susceptible	The MTB strain isolated was susceptible to rifampicin therefore patient has rifampicin susceptible TB	This does not exclude the possibility of resistance to other first line drugs i.e. INH, PZA, E
Rifampicin resistant	The MTB strain isolated was resistant to rifampicin therefore the patient has rifampicin resistant TB,	This does not mean the patient is also resistant to Isoniazid therefore has MDR-TB. The patient has Rifampicin mono resistance (RR-TB).

4.1.2 Follow up of patients after receiving laboratory results

- Patients must be given a return date within two days for the results and treatment initiation.
  - If the results confirm drug susceptible TB, the patient should be counselled, started on treatment (Regimen 1, irrespective of patient category) and another sputum specimen collected on spot for baseline microscopy. The patient does not need to come back for the results but the results should be filed and documented in the patient's clinic record.
  - If the results confirm drug resistant TB, the patient should be counselled and arrangements for referral to the MDR-TB treatment initiation site made. The clinical assessment, confirmatory and baseline tests will be conducted at the treatment initiation site. Only a small percentage of Xpert rifampicin resistant tests may be false positive i.e. confirmatory testing may show rifampicin susceptible, therefore a RR-TB result should not be barrier to treatment.
- If a patient does not return on the specified date and the results confirm drug susceptible or drug resistant TB they should be traced and started on treatment as soon as possible.
- For all patients with infectious TB (drug susceptible/ resistant) contact and source investigation must be conducted.

Contacts of smear positive patients must be prioritised.

4.2 LINE PROBE ASSAY DIAGNOSTIC ALGORITHM

The LPA test may be used on high risk patients where rapid diagnosis of MDR-TB or Isoniazid resistance is required. One spot sputum specimen should be collected for smear microscopy, if AFB positive then another specimen must be collected for LPA. If smear microscopy is AFB negative, another smear for culture and LPA must be collected.

4.2.1 Interpretation of the LPA results

Result	Action
Smear microscopy results are AFB positive	The LPA test will be conducted on the second specimen and the results should be back within 5 – 7 days, therefore the patient should be given a return date within 7 days. If the results confirm drug resistant TB the patient should be counselled and arrangements for referral to the local MDR-TB Unit made to ensure treatment initiation as soon as possible. If the results confirm drug sensitive TB, the patient should be counselled and started on TB treatment immediately.
Smear microscopy results are negative	If DR-TB is strongly suspected then a second specimen for culture must be collected for culture and LPA. Whilst waiting for results, chest x-rays may be conducted to support the diagnosis. If clinical and x-ray findings are suggestive of TB, the patient may be started on Regimen 1 and the results reviewed as soon as available and patient managed appropriately

Result	Meaning	Action
MTB complex detected	MTB was isolated from the specimen therefore the patient has bacteriologically confirmed TB	Review susceptibility results and treat accordingly
MTB complex not detected	MTB was not isolated from the specimen	This result does not completely exclude TB
Rifampicin and Isoniazid susceptible	Patient has drug susceptible TB	Treat with Regimen 1
Rifampicin and Isoniazid resistant	Patient has multi drug resistant TB (MDR-TB)	Treat with Category IV
Rifampicin resistant and Isoniazid susceptible*	Patient has Rifampicin mono resistance (RR-TB)	Treat with Category IV
Rifampicin susceptible and Isoniazid resistant	Patient has Isoniazid mono resistance	Treat with first line drugs RHZE for 6 months

* Isoniazid resistance is more complex genetically than rifampicin resistance. The LPA can "miss" isoniazid resistance (i.e. report a false isoniazid susceptible result). In most laboratories, if the LPA shows rifampicin mono resistance, the isoniazid susceptibility will be tested on phenotypic drug susceptibility testing for confirmation.

4.3 Baseline evaluation of TB patients

Investigations		Recommended frequency
Microscopy	All patients	Baseline, 7 weeks and 23 weeks
Height	All patients	Baseline
Weight	All patients	Baseline and monthly
Body mass index	All patients	Baseline
HIV test	Patients with unknown HIV status or have not tested in the past year	Baseline
Blood glucose	Urine glucose and ketones (All patients)	Baseline
	Blood glucose (symptomatic patients)	Baseline and monthly for diabetic patients
Pregnancy test	Women of child bearing age, presenting with history of amenorrheoa and not on contraception	Baseline
Alcohol use screening	Patients with a history of alcohol use	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
Chest x-ray	Patients with concomitant lung disease and those with a history of working in the mines	Baseline, end of treatment

4.4 Screening TB patients for diabetes

All TB patients must be screened for symptoms of diabetes namely polydipsia, polyuria and weight loss. Other symptoms include blurring of vision, general body weakness and lethargy, poor wound healing. If any of these symptoms are present a random or fasting blood glucose test must be conducted.

A diagnosis of diabetes is made when the random blood glucose is ≥ 11.1 mmol/L in the presence of symptoms or fasting blood glucose is ≥7 mmo/L. Patients must be managed as outlined in the guidelines for the "Management of Type 2 Diabetes in Adults at primary care level".

Urine dipstick test must be routinely conducted on all newly diagnosed TB patients to screen for diabetes and all patients with abnormal results investigated further for diabetes.

5. REGISTRATION OF TB PATIENTS

The diagnosis of TB refers to the recognition of an active TB disease due to Mycobacterium tuberculosis in a patient. Beyond making the diagnosis of TB, it is also necessary to categorise the TB patients for appropriate treatment and to evaluate the treatment outcomes in a standardised manner. Defining the different registration classifications of patients is essential for proper notification, standardisation of the treatment for the registration types, evaluation of trends in notifications and cohort analysis of treatment outcomes. The registration type is determined by site of the disease, bacteriology, severity of TB disease and history of previous treatment of TB.

Bacteriologically confirmed Tuberculosis

A patient with Mycobacterium tuberculosis complex identified from a clinical specimen, either by smear microscopy, culture or molecular assays

TB patient (person with tuberculosis)

A person who has been diagnosed with bacteriologically confirmed TB or started on TB treatment by a health care worker based on clinical presentation, x-rays findings or other tests

5.1 Site of TB disease

	Definition	Comment
Pulmonary TB	Disease involving the lung parenchyma.	- A patient with both a parenchymal lesion in the lungs (pulmonary TB) and extra-pulmonary TB is classified as pulmonary TB.
Extra-pulmonary TB	Disease involving organs other than the lungs: e.g. pleura, lymph nodes, abdomen, genito-urinary tract, skin, joints and bones and meninges	- 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.

5.2 Bacteriology results (bacteriological confirmation)

Category	Definition	Comment
Xpert positive TB	A positive Xpert result or MTB detected in at least one specimen tested.	This applies to both pulmonary and extra pulmonary specimen
Xpert negative TB	A negative Xpert result or MTB not detected in at least one specimen tested	This applies to both pulmonary and extra pulmonary specimen
Smear positive PTB	A positive Xpert result and at least 1+ acid-fast bacilli (10-99 AFB per 100 oil immersion fields) in at least one sputum smear microscopy	This is essential for contact investigation and monitoring the patient's response to treatment as well as confirming cure.
Smear negative PTB	A positive Xpert result and at least one sputum smear microscopy negative for AFBs	This may be used to monitor the patient's response to treatment
Culture positive TB	A positive culture result with or without a Xpert result.	This applies to both pulmonary and extra pulmonary specimen.
This is essential for contact investigation and maybe used for confirming cure.		

NOTE: LPA results are considered bacteriological confirmation but since the test is conducted on smear microscopy or culture positive specimen it is not reflected

Where the sputum smear microscopy was not done at baseline it must be recorded as such.

5.3 Clinically diagnosed TB

People who are started on TB treatment without bacteriological confirmation of disease. This includes patients started on treatment based on;

- chest x-ray abnormalities that are consistent with active TB
- the history and clinical picture suggestive of PTB or EPTB
- histological and biochemical tests suggestive of TB

5.4 Severity of disease

The extent of the disease and the anatomical site determine the severity of disease and duration of treatment. Disease is considered to be severe if there is a significant, acute threat to life and / or risk of serious long-term consequences.

5.5 History of previous treatment

The purpose of classifying patients according to previous TB treatment is to identify those patients at increased risk of acquired drug resistance and to manage them appropriately. This is also important for monitoring of the TB epidemic and programme performance. The different categories are as follows:

Category	Definition
New:	A patient who has never had treatment for TB or who has taken anti-tuberculosis drugs for less than 4 weeks. They may have Xpert, smear, culture positive/ negative PTB or EPTB.
Previously treated (Re-treatment)	A patient who has taken TB treatment for 4 weeks or more in the past and either relapsed, defaulted or had treatment failure. They may have positive or negative Xpert, smear and culture PTB or extra pulmonary TB disease.
Relapse	A patient who received treatment and was declared cured or treatment completed at the end of the treatment period and has now developed TB again. ***These patients could be true relapses or have a new episode***
Re-treatment after failure	A patient who received treatment and remained or became smear or culture positive at the end of the treatment period.
Re-treatment after default	A patient who completed at least one month of treatment and returns after interrupting treatment for two months or more.
Other previously treated	A patient who was previously treated but the outcome of previous TB treatment is unknown
Patients who do not fit any of the above categories are classified as "unknown previous TB treatment".	
Transfer in	A patient who has been diagnosed and registered for treatment in a facility in one district and is transferred to a facility in another district to continue treatment. *The smear conversion and treatment outcome for this patient must be reported back to the facility that transferred the patient.*
Electronic TB register case definitions: **These are used mainly for the ETR, to clearly define cohorts at district level and avoid duplication of patient records and double counting.**	
Newly Registered	A patient who is diagnosed and registered for treatment in a facility
Moved in	A patient who is diagnosed and registered for treatment in one facility and is referred to another facility within the same district to continue treatment. *The smear conversion and treatment outcome for this patient must be reported by the receiving facility*
Moved out	A patient who is referred from a facility where the diagnosis and registration for treatment was made, to another facility, within the same district to continue treatment. *This is not an outcome but serves to match patients moving within a district in order to prevent double counting.*

5.5 Treatment outcome definitions for smear/ culture positive PTB

Outcome	Definition
Cure	Patient whose baseline smear (or culture) was positive at the beginning of the treatment and is smear/ culture negative in the last month of treatment and on at least one previous occasion at least 30 days prior.
Treatment completed*	Patient whose baseline smear (or culture) was positive at the beginning and has completed treatment but does not have a negative smear/ culture in the last month of treatment and on at least one previous occasion more than 30 days prior. *The smear examination may not have been done or the results may not be available at the end of treatment.*
Treatment failure	Patient whose baseline smear (or culture) was positive and remains or becomes positive again at 5 months or later during treatment. *This definition excludes those patients who are diagnosed with RR-TB or MDR-TB during treatment.*
Died	Patient who dies for any reason during the course of TB treatment.
Treatment default	Patient whose treatment was interrupted for two consecutive months or more during the treatment period.
Transfer out	Patient who was referred to a facility in another district to continue treatment and for whom the treatment outcome is not known.

*Treatment success is a combination of the patients who were cured and those who completed treatment.

5.6 Treatment outcome definitions for patients with EPTB, smear/ culture negative PTB

Outcome	Definition
Treatment completed	Patients who were initially diagnosed as EPTB (with or without bacteriological confirmation), patients diagnosed with PTB whose baseline smear (or culture) result was negative and those started on treatment based on clinical and radiological findings who have shown clinical improvement and completed the prescribed course of treatment
Treatment failure	Patients who were initially diagnosed as EPTB (with or without bacteriological confirmation), patients diagnosed with PTB whose baseline smear (or culture) result was negative and those started on treatment based on clinical and radiological findings, who have not shown clinical improvement or became smear (or culture) became positive or their condition deteriorated during the course of treatment *This definition excludes those patients who are diagnosed with RR-TB or MDR-TB during treatment.*
Died	Patient who dies for any reason during the course of TB treatment.
Treatment default	Patient whose treatment was interrupted for two consecutive months or more during the treatment period.
Transfer out	Patient who was referred to a facility in another district to continue treatment and for whom the treatment outcome is not known.

6. CONTACT INVESTIGATION

The investigation of people exposed to patients with infectious tuberculosis is one of the priorities of the TB control programme. Close contacts of people with active pulmonary tuberculosis are at increased risk of acquiring infection, developing active disease and spreading it. Timely identification and adequate treatment of those with active pulmonary tuberculosis reduces the risk of exposure of community members. As a result, the incidence of tuberculosis will be diminished, as the prevalence of infection with Mycobacterium tuberculosis declines over time.

The objectives of contact investigation are as follows:

1) to reduce morbidity and fatality due to tuberculosis by early identification and adequate treatment of further cases of active tuberculosis among contacts of index cases with active tuberculosis;
2) to arrest further transmission by early detection of possible (secondary) cases;
3) to prevent future cases of tuberculosis in the population by detection and preventive therapy of infected high risk contacts (children, immune compromised individuals) of index cases with active tuberculosis;

The aims of contact tracing in the context of a single index patient of drug susceptible TB are:

a) To identify contacts with active TB disease and initiate treatment early
b) To identify those at high risk of developing active tuberculosis/severe outcomes, i.e. young children and immune compromised persons, to prevent the development of TB by providing IPT.
c) Identify all close household contacts of MDR/ XDR-TB, without active disease for monitoring for 2 years after disease onset in index patient
d) To provide individual/ family education on infection control and counselling

6.1 Definition of contacts

These are people who share the same air for prolonged periods of time with people who are coughing up the MTB into the air (smear or culture positive PTB) and are therefore at risk of getting infected. This applies not only to households but to hostels, prison cells boarding schools, and homeless shelters. The “8 hour” cut-off is used for pragmatic reasons and in specific settings of presumed increased risk such as outpatient departments, general/ TB wards or while conducting sputum inducing procedures, frequent but intense contact of less than 8 hours may be considered to pose similar risk as above.

6.2 Initiating contact investigation

Every new patient diagnosed with laboratory confirmed PTB should trigger a contact investigation. Only patients with infectious pulmonary tuberculosis warrant the initiation of contact tracing. They should be interviewed promptly after diagnosis to assess the need for, and the urgency of, contact investigation based on infectiousness and whether they have drug susceptible TB or drug resistant TB.

In order to determine the contacts, the period of infectiousness of the patient has to be estimated. Since this is not always possible a rough estimate can be made based on the date of onset of cough.

The risk of transmission of infection is determined by;

- The infectiousness of the index patient (i.e. person with smear positive PTB)
- Duration of exposure (i.e. spending at least eight continuous hours with the index patient)
- The environment in which the exposure is suspected to have occurred (i.e. poorly ventilated room)

6.3 Prioritisation of contacts

The urgency of contact investigation will depend on the degree of infectiousness of the index patient, whether they have DS-TB or DR-TB and the immunity of contacts (children< 5years, immunocompromised people). The following situations should receive priority for contact tracing;

- Where the index patient is "sputum smear-positive" have the highest potential of being transmitters.
- Where the index patient has MDR-TB
- Where there are children or immune compromised people among household contacts

6.4 Interviewing index patients

After confirmation of the diagnosis and starting the index patient on treatment, the nurse or doctor should take time to inform the patient about the disease, how it is acquired and spread, their treatment journey, the importance of treatment adherence and discuss treatment and care options that will suit the patient.

The index patient should be interviewed about their social network and their activities during the period of infectiousness in order to identify contacts that may also have active disease. In addition the interviewer should explain the contact tracing procedures that will be followed, including contact tracing slips and home visits. Patients should be assured that apart from the need to disclose to contacts that they have been exposed to TB, confidentiality regarding other aspects of their disease management will be ensured. Information about close contacts should be obtained from the patient and a list of all appropriate contacts compiled.

Patients should be advised to inform the contacts identified that may also have active disease to expect a contact slip, call and/or home visit from the community health worker.

The information on contacts should include the name, age, residential address during the period of illness of index patient and contact details. This information must be recorded in the Patient Treatment Record (GW 20/12). The interviewer should complete the contact notification form (Annexure 6), explain the purpose of the form to the index patient and ask him/her to pass them on to the named contacts. This form must be presented to any clinic for screening and testing. The feedback must be provided to the referring facility by completing the bottom section of the form. The interviewer should record in the Patient Treatment Record (GW 20/12) that contact form were given to the index case.

6.5 Assessment of contacts during a home or clinic visit

The assessment of potential contacts should involve the following domains;

1) **Symptom screening:** Contact is screened for TB symptoms (cough, sweating at night, fever and loss of weight), and if any of the symptoms are present, they should be asked to provide sputum for investigation and a follow up clinic visit should be scheduled. All symptomatic contacts that are investigated for TB must be entered in the TB Identification and Follow up Register (GW 20/13).
2) **Investigations:** If contact is coughing, one sputum specimen must be collected for Xpert testing. Those who are not coughing or cannot produce sputum but are symptomatic must be referred to the clinic/ hospital for investigation.
3) **Risk factor assessment:** The person should be assessed for the risk factors for development of TB disease (e.g. age < 5years, HIV positive, diabetes, malnutrition). HIV testing must be offered and diabetic screening conducted. All children less than 5 years must be assessed for nutritional status.

4) **Environmental assessment:** An environmental assessment can be done and information provided on how to prevent TB transmission through appropriate environmental interventions.

The CHW or health worker should record in the Patient Treatment Record (GW 20/12) of the index patient that contact tracing and screening was done and subsequent actions.

6.6 Assessment of contacts during outbreaks

Outbreak cases can be distinguished from other cases only when certain association in time, location, patient characteristics, or M. tuberculosis attributes (i.e. drug resistance or genotype) become apparent. In South Africa, clusters are likely to be obscured by the baseline incidence until suspicion is triggered by a noticeable increase, a sentinel event (i.e. paediatric cases), or genotypically related MTB isolates. During outbreaks, contacts can be exposed to more than one case, cases and contacts can be interrelated through multiple social connections which complicate control efforts. Therefore, the implications of an "outbreak", once declared are the mobilization of additional resources to control it, and bring the situation back to "normal". Therefore, the most critical initial step is to confirm the existence of an outbreak.

Outbreaks are defined as the observation of more cases than expected in time and place. For TB this can be extended to an increase in associated morbidity, or an increase in associated resistance. To assess either of these, a baseline of incidence, morbidity or resistance needs to be established. For example, if 2 cases are identified among pupils in a specific class, within a 2 month period, this is on its own not enough to declare an outbreak. The health care workers need to look at retrospective data to ascertain if 2 pupils with TB in a class, over a 2 month period is more than one would expect over a similar period, based on historical data.

Once an outbreak is confirmed, based on the above definition, the next step is to ascertain if this outbreak is caused by a unique strain of TB, or by the increase in incidence of a common strain. To do this, extra specimen need to be collected by the health care workers from the affected patients for strain typing. The risk factors contributing to a specific outbreak should be determined, because these findings will affect the investigation and inform the strategy.

6.7 Initiating an outbreak response

The provincial TB Program Manager after consultation with district coordinator and the district management team can declare a TB outbreak and initiate an outbreak response plan. This decision to will be based on the criteria for defining an outbreak mentioned above.

The aim of the outbreak response is to;

- Identify all TB cases using the contact definitions above
- Initiate appropriate treatment and ensure follow up

6.8 Confidentiality and consent in contact investigations

Maintaining confidentiality is challenging during contact investigations because of the social connections between an index patient and contacts. Constant attention to maintaining confidentiality is required. Ongoing discussions with the index patient and contacts regarding confidentiality are helpful in finding solutions, and individual preferences often can be accommodated.

Legal and ethical issues in sharing confidential information sometimes can be resolved by obtaining consent from the patient to disclose information to specified persons and by documenting this consent with a signed form. Informed consent for disclosure of information in the patient's primary language is recommended. Refusal to grant consent can threaten public health and requires documentation and sometimes legal consultation for determining acceptable interventions.

7. PRINCIPLES OF TB TREATMENT

The key to stopping the spread of TB in a community is to start treating patients who are coughing up live TB bacilli as soon as possible. Apart from the public health imperative, effective treatment reduces individual morbidity and mortality. For treatment to be effective, it is crucial that the correct drugs are given for the correct period of time. PTB and EPTB are both treated in the same way.

The aims of TB treatment are to:

- Cure the patient of TB
- Decrease transmission of TB to others
- Prevent the development of acquired drug resistance
- Prevent relapse
- Prevent death from TB or its complications

7.1 The essential TB drugs

TB drugs have varying properties:

1) They may be bactericidal, bacteriostatic (sterilising) or have the ability to prevent resistance.
2) They differ in the ability to act against the various populations of bacilli found in a tuberculosis lesion:
   - Metabolically active bacilli, intermediately active bacilli, semi-dormant bacilli (persisters), which undergo occasional spurts of metabolism and dormant bacilli (that may become active).
   - Some TB drugs act best in an acid environment; others better at a more alkaline pH
3) Bacilli occur both in extracellular spaces where the pH is usually neutral or alkaline and in intracellular spaces where it is acid.

Table 7.1: Properties of the individual TB Drugs

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

7.2 Standard treatment protocols

Standardised treatment protocols with fixed dose combination medicines are used for TB treatment. There are now three treatment regimens;

Regimen 1: for new and previously treated adults and children >8yrs/ >30kg
Regimen 3A: for children < 8yrs and <30kg with uncomplicated TB disease
Regimen 3B: for children < 8yrs and <30kg with complicated TB disease

Table 7.2: Recommended daily dosages of the individual drugs for adults and children >8yrs/ >30kg

Essential TB drug (abbreviation)	Dose mg/kg	Dose range mg/kg
Rifampicin (R)	10	8 – 12
Isoniazid (H)	5	4 – 6
Pyrazinamide (Z)	25	20 – 30
Ethambutol (E)	15	15 – 20
Streptomycin (S)	15	12 – 18

Table 7.3 : Fixed dose combination tablets available for adults and children >8yrs/ >30kg

Intensive Phase	Continuation Phase
RHZE (150,75,400,275mg)	RH (150,75mg) RH (300,150mg)

7.3 Standard treatment regimen for New and Previously treated patients

The standard treatment regimen for all patients is made up of an intensive phase lasting 2 months and a continuation phase lasting 4 months. During the intensive phase 4 drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) are used to rapidly kill the tubercle bacilli. Infectious patients become less infectious within approximately 10-14 days of starting treatment and symptoms abate. However, the majority of patients with sputum smear-positive TB will become smear-negative within 2 months. In the continuation phase, 2 drugs (isoniazid, rifampicin) are used, over a period of 4 months. The sterilizing effect of these drugs eliminates the remaining bacilli and prevents subsequent relapse.

7.3.1 Regimen 1: 2(HRZE) / 4(HR)

During the first two months, treatment is with isoniazid, rifampicin, pyrazinamide and ethambutol in fixed dose combinations given 7 days a week. If the patient is smear negative and clinically improving at the end of the second month they are treated with isoniazid and rifampicin in fixed dose combinations given 7 days a week for four months.

REGIMEN 1: FOR ADULTS AND CHILDREN OLDER THAN 8 YEARS OR WEIGHING MORE THAN 30KG

Pre-treatment body weight	**Intensive Phase** 7 days a week for 2 months	**Continuation phase** 7 days a week for 4 months	
	RHZE (150,75, 400,275)	**RH (150,75)**	**RH (300,150)**
30-37 kg	2 tabs	2 tabs	
38-54 kg	3 tabs	3 tabs	
55-70 kg	4 tabs		2 tabs
>70kg	5 tabs		2 tabs

7.4 Treatment for Extra pulmonary TB

Six months treatment is as effective in extra-pulmonary as in pulmonary disease. 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 two months and the continuation phase is prolonged to seven months – 2(RHZE)/ 7(HR).

7.5 Adjunctive treatment

7.5.1 Pyridoxine (Vitamin B6)

The use of Pyridoxine is recommended for all adults patients started on TB treatment to prevent peripheral neuropathy most commonly caused by Isoniazid.

Dose of Pyridoxine: 25mg daily

If patient develops peripheral neuropathy at any stage during TB treatment, the dose can be increased to 50 – 75mg (up to maximum of 200mg) until the symptoms subside, then reduce to 25mg daily.

7.5.2 Steroids

The use of corticosteroids is recommended in extra-pulmonary tuberculosis, particularly for TB meningitis and pericarditis. High dose steroid treatment for 2-4 weeks and the taper off gradually over several weeks depending on clinical progress is recommended.

The response to treatment is assessed clinically.

NO TRIALS OF THERAPY SHOULD BE GIVEN.

Effective treatment of TB requires adherence to the TB treatment short-course. Adequate dosing and duration of treatment is important for cure. To ensure this, dosages must be adjusted at the end of intensive phase where the weight has changed.

8. MANAGEMENT OF THE COMMON SIDE EFFECTS OF TB MEDICINES

8.1 Monitoring for side effects

The clinical monitoring of all TB patients for side effects during treatment is important. Key to this is educating the patients and their families on how to recognise the symptoms of the common side effects and to report them immediately when they develop. At every follow up visit, the patients must be asked about the following symptoms;

- Burning, numbness and tingling sensation in the feet
- Joint pains
- Anorexia
- Nausea
- Abdominal pains
- Skin rash with/ without itching
- Changes in the colour of urine
- Impaired vision
- Yellowing of eyes
- Confusion

When the patient has minor side effects they can be reassured and treated symptomatically at the clinic. When they present with major side effects they must be referred to next appropriate level of care – hospital immediately.

Table 8.1: Common side effects of TB drugs

Side effects	Drug(s) responsible
Minor	
Anorexia, nausea, abdominal pains	Rifampicin
Joint pains	Pyrazinamide
Burning sensation in feet	Isoniazid
Orange/ red coloured urine	Rifampicin
Major	
Skin itching/ rash	Streptomycin, Rifampicin, Isonazid
Deafness (no wax on otoscopy)	Streptomycin
Dizziness (vertigo, nystagmus)	Streptomycin
Jaundice (other causes excluded)	Isoniazid, Rifampicin, Pyrazinamide
Vomiting, confusion	Isoniazid, Rifampicin, Pyrazinamide
Visual impairment/ loss	Ethambutol
Generalised purpura, shock and purpura	Rifampicin

8.2 Medicine induced hepatotoxiciy

Isoniazid, rifampicin and pyrazinamide are all associated with hepatitis. Of the three, rifampicin is least likely to cause hepatocellular damage, although the drug is associated with cholestatic jaundice. The most common cause of liver toxicity is Isoniazid followed by Pyrazinamide. Ethambutol is the only safe drug to use in people with liver disease. People at high risk of developing liver toxicity are those with a

history of alcohol abuse, chronic liver disease (cirrhosis, hepatitis) and patients older than 35 years (the incidence of liver toxicity increases with age)

The risk factors for medicine induced liver disease include the following;

- Pre existing liver disease i.e. alcohol liver disease, co-infection with Hep B/C
- Concomitant hepatotoxic medicines such as amiodarone, paracetamol, cotrimoxazole
- HIV associated hepatobiliary disease
- Genetic predisposition

Hepatotoxicity occurs most commonly in first 2 months but occasionally can occur later. Patient may present with nausea, vomiting and abdominal discomfort. They may or may not have jaundice and could present with fulminant hepatic failure. All patients presenting with symptoms and signs of hepatotoxicity must be referred to the hospital for further investigation and management.

8.2.1 Hepatitis

Clinical features

The symptoms include:

- Anorexia
- Fatigue
- Nausea and vomiting
- Mild fever
- Tender enlargement of the liver
- Jaundice (yellowing of the eyes or skin)
- Dark urine

Investigations

Liver function test abnormalities include;

1. Increase in AST/ALT

   If the ALT is elevated > 5 times upper limit of normal (ULN), it indicates liver cell damage (hepatitis)

   An elevated AST is not specific for TB and therefore other causes of the increased AST must be excluded

2. Disproportional increase in alkaline phosphatise (ALP) and total Bilirubin levels is most commonly seen in Rifampicin hepatotoxicity.

8.2.2 Cholestasis

The most likely causes of this include;

- Biliary obstuction
- Medicines – Rifampicin, neveripine
- Recovery state from recent acute viral hepatitis
- Sepsis
- HIV
- Cholangitis
- Cholangiopathy
- Liver infiltration TB/Lymphoma
- Reconstitution syndrome

Liver function test abnormalities include;

- elevated Bilirubin levels (>50%)
- elevated ALT/AST (often >5X ULN).

Other useful additional investigations

- Bloods: Coagulation profile, Hepatitis ABC
- Ultrasonography to exclude obstruction/features in keeping with disseminated TB (liver abscesses, splenic micro abscesses, para aortic lymphadenopathy).

8.3 Management of medicine induced hepatotoxicity

- Rule out other causes such as excessive alcohol use, other medication the patient might be taking, pre existing liver disease and viral hepatitis
- Stop all medicines the patient is taking - the combination TB treatment (RHZE or RH), cotrimoxazole, ART
- Conduct liver function tests, serological testing for Hepatitis A, B and C (for patients who are high risk for hepatitis) and HIV test (if status is not known)
- Monitor the clinical symptoms until they resolve
- Monitor the ALT until the levels are less than 100 IU/l and Bilirubin levels normal.
- Start Rifampicin 10mg/kg/day (max 600mg/ day)
- Repeat ALT on day 3,
- If normal, add Isoniazid 5mg/kg/day (max 300mg/ day) on day 4 to 6
- Repeat ALT on day 7,
- If normal, add Ethambutol 15mg/kg/day on day 8-10
- Check ALT on day 10,
- If normal consider Pyrazinamide 25mg/kg/day (if patient is in intensive phase of treatment) and continue as per Regimen 1, repeating ALT weekly for a month

8.4 Treatment for patients who cannot tolerate one of the first line medicines

- If patient cannot tolerate Isoniazid: Treat with Moxifloxacin/ Rifampicin/ Ethambutol for 12 months (Pyrazinamide may be added during the intensive phase).
- If patient cannot tolerate Rifampicin: Treat with Moxifloxacin/ Isoniazid/ Ethambutol for 18 months (Pyrazinamide or Streptomycin maybe added during the intensive phase).
- If patient cannot tolerate Rifampicin and Isoniazid: Treat with Moxifloxacin, Ethambutol and Streptomycin for 18 months.
- If patient cannot tolerate Pyrazinamide: Treat with Rifampicin/ Isoniazid/ Ethambutol for 9 months.
- If the patient is severely ill due to TB, and stopping treatment is not an option, a liver friendly regimen comprising Ethambutol, Moxifloxacin and Streptomycin can be started. This can be stopped if the patient is ready to be re challenged with Rifampicin, Isoniazid (or both).
- Reintroduce Cotrimoxazole after TB treatment once liver function tests are acceptable, if they deteriorate consider changing to Dapsone.

8.5 Gastro-intestinal intolerance

The drug most commonly associated with gastro-intestinal intolerance is rifampicin. The symptoms usually occur within the first few weeks of treatment and are:

- Nausea, vomiting
- Poor appetite
- Mild abdominal pain
- Diarrhoea occurs less frequently.

Management

- Exclude other possible causes of GI intolerance such as alcohol intake, non steroidal anti-inflammatory drugs
- Ask patient about history of gastritis, gastric ulcers, gastro-esophageal reflux, pancreatitis etc
- These are managed symptomatically as they are mild.
- Consider changing the time for drug administration, taking medication just before or after a meal or with a light snack or at bedtime

- Give antacid, anti emetic, antidiarrhoeal depending on the severity of symptoms. Patient should be advised not to take the antacid 1 hour before and 2 hours after taking treatment as the aluminium reduces INH bioavailability.
- If symptoms persist refer for further investigation.

8.6 Peripheral neuropathy

The main cause of peripheral neuropathy is Isoniazid. It occurs more commonly in patients who are malnourished, diabetics, abuse alcohol, patients with renal failure, pregnant women and breastfeeding mothers and HIV positive patients, including those patients on ART

Symptoms and signs
Tingling/ burning sensation and numbness of the hands and feet

Management
- This can be treated by giving the patient Pyridoxine 50 – 75mg daily, the recommended dose for HIV positive patients is 100mg daily.
- The patient must be informed about the causes of the side effects and the benefits of taking pyridoxine.

Prevention
In the high risk groups, peripheral neuropathy can be prevented by adding Pyridoxine to the TB treatment. The recommended dose is 25 mg daily.

8.7 Optic neuritis

Progressive loss of vision caused by retrobulbar neuritis usually manifests first as loss of colour vision and usually presents after the patient has been on treatment for at least two months. This is usually caused by excessive doses of ethambutol. Ethambutol should not be given if there is pre-existing optic neuritis

Symptoms and signs
- Reduced red-green color discrimination
- Blurred vision
- Difficulty in reading
- These may occur in one or both eyes

Management
Stop the treatment immediately and introduce individual drugs (excluding Ethambutol)

8.9 Rash

All TB drugs can cause rash. The management of the rash depends on the severity

Type of rash	Management
Mild itching rash	1) Give antihistamine 2) Prednisone may be added at 40mg/day and tapered gradually as the rash clears 3) A topical cream may be added
Petechial rash	1) Mainly due to Rifampicin 2) Conduct Platelet count 3) If below normal range (150,000 – 450,000 per microliter), stop Rifampicin and exclude from regimen. 4) Monitor platelet count until it returns to normal
Erythematous rash with fever	1) Stop all drugs 2) Rule out anaphylaxis reaction which can be characterised by any of the following – angioedema, swollen tongue/ throat, flushed face, airway constriction, wheezing, difficulty in breathing, hypotension 3) If treatment cannot be interrupted due to severity of disease, a regimen comprising other drugs the patient has not used can be started (Streptomycin/ amikacin/ kanamycin/ ofloxacin/ levofloxacin/ cycloserine) 4) If rash improves, the drugs can be re introduced one by one every 2-3 days starting with Rifampicin which is potent and least likely to cause the rash, followed by Isoniazid, then pyrazinamide and ethambutol. 5) Monitor the signs and symptoms and if rash recurs at any point the last drug added should be stopped.

9. MONITORING THE RESPONSE TO TREATMENT

Appropriate monitoring of the response to treatment is important for the clinical care of all categories of TB patients. While molecular tests for TB have improved TB diagnosis, these tests have not been validated for monitoring. Therefore, patients with bacteriological confirmation of pulmonary tuberculosis must be assessed clinically and bacteriologically to monitor their response to treatment.

All patients diagnosed with Xpert must have a baseline smear result and followed up accordingly;

- Patients with smear-positive PTB are monitored by sputum smear examination
- Patients with smear-negative PTB are monitored by sputum smear examination
- Patients with EPTB and those without bacteriological confirmation of TB disease are monitored clinically

9.1 Bacteriological monitoring

One sputum specimen is taken on the spot during the course of PTB treatment to evaluate the bacteriological response to treatment. There should be no interruption to treatment whilst smears are evaluated. The dates on which these sputa are due must be clearly indicated in the patient's blue clinic folder and patient-held green card to serve as a prompt to both staff and patients. Timely collection of sputa from patients ensures that they are treated appropriately based on the results and also help to determine their treatment outcomes.

If there is poor response to treatment, drug resistance should be excluded through Xpert, LPA, culture and drug susceptibility testing. Patients may appear to not respond to treatment despite being susceptible on Xpert or LPA and treatment compliant due to being infected with unusual strains. Please contact a pathologist to discuss appropriate further testing.

9.2 Clinical monitoring

Patients with extra-pulmonary TB or those who were diagnosed on clinical grounds without bacteriological confirmation of TB should be monitored clinically over the duration of treatment. Weight is a useful indicator of clinical improvement therefore it should be monitored monthly. If there is poor response to treatment, alternative diagnoses and the possibility of drug resistance must be considered.

Timing of sputum examination	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 health care worker on whether to change the patient to continuation phase of treatment or extend the intensive phase	1) **If negative**, change to the continuation phase of treatment at the end of the 8th week of intensive phase treatment. 2) Register the patient as "negative"	This means the patient is responding well to treatment Educate and counsel patient about importance of treatment compliance
		3) **If positive**, check for treatment compliance, re-assess patient clinically a) Conduct LPA (or culture and DST, if LPA is not available) b) Continue with the intensive phase treatment for one month c) Register the patient as "positive" d) Review the drug susceptibility results when available	This indicates the following: • That the initial phase of therapy was poorly supervised and that patient's compliance to treatment was poor. • That there is a slow rate of progress with smear conversion, which is common in patients with extensive cavitations and a high bacillary load at diagnosis. • That the patient may have resistance to the other TB drugs i.e. Isoniazid (since only Rifampicin resistance was excluded upfront) or may have been re-infected with a drug resistant strain. • The patient could have Non Tuberculous Mycobacterial infection • The patient may have another condition or taking other medication that affects the absorption or effectiveness of the TB drugs • Patient may have been infected with mixed strains with amplification of resistant strains due to treatment Address treatment compliance by counselling the patient and identifying a treatment supporter where necessary

For those remaining positive at 2 months			
Repeat smear one week before the end of the 3rd month (11 weeks)		4) **If negative and drug susceptible**, change to continuation phase of treatment at the end of the 12th week. Register the patient as "negative" 5) **If negative and Isoniazid mono resistant TB is confirmed**, continue intensive phase treatment and refer patient to MDR-TB for assessment and registration in DR-TB register. Register the patient as "Isoniazid mono resistant TB" in the TB register 6) **If still positive and RR-TB or MDR-TB is confirmed**, stop treatment and refer patient to the MDR-TB treatment initiation site for assessment and treatment initiation. Register the patient as "RR-TB or MDR-TB" in TB register.	The intensive phase treatment is not extended beyond three months in patients with drug susceptible TB
END OF CONTINUATION PHASE			
One week before the end of the 4 months continuation phase (at 23 weeks)	To determine the final outcome of treatment for the patient.	1) **If negative,** stop treatment at the end of the 24th week of treatment. Register the patient as "cured"	Educate the patient about TB prevention and healthy lifestyle
		2) **If positive**, stop TB treatment. Register patient as "treatment failure" a) Conduct LPA and DST for pyrazinamide and ethambutol b) Review the results when available.	This indicates the following: • That the patient was re-infected with a sensitive or resistant strain. • The treatment during the continuation phase was unsupervised and patient compliance was poor
For those remaining positive at 6 months			
	To determine further management of the patient	1) **If drug susceptible**, re-start TB treatment, counsel the patient and provide treatment support.	
		2) **If DR-TB (RR-TB, INH Mono resistant, MDR-TB, Other resistance)**, refer to the MDR-TB treatment initiation site hospital for assessment and treatment.	

10. ADHERENCE TO TREATMENT

The aim of the TB programme is to successfully treat all patients started on treatment. This can only be achieved by ensuring good compliance to treatment. TB is curable if patients take a complete and uninterrupted course of the appropriate drug therapy. However, poor compliance to TB medication is a common problem. Treatment interruption presents a problem for patients, for their family and community and for the health care personnel caring for them. The consequences of inadequate and incomplete treatment are serious:

- Prolonged illness and disability for the patient.
- Infectiousness of the patient causing continued TB transmission in the community.
- Development of drug resistant TB.
- The possibility of death.

TB is a complex disease that has biological, social, economic and cultural implications for the patient. Health care providers should be mindful of the strong impact that TB can have on all aspects of the patient's life. Due consideration should be given to the many factors that can adversely influence treatment outcomes.

Table 10.1 Factors that Influence Treatment Outcomes

Social and Economic Factors	**Health System Factors**
• Extreme poverty • Poor support networks • Unstable living circumstances • Substance abuse • Beliefs about TB and its treatment	• Poor health infrastructure • Poorly trained or supervised health care personnel • Low levels of accountability of health staff • Poor relationships with patients • Inadequate development of community based support for patients
Patient related factors	**Therapy related factors**
• Stigma • Depression • Disempowerment • Poor knowledge about TB and the efficacy of treatment	• Complex treatment regimens • Large pill burden • Adverse effects of medication • Long treatment duration.

A comprehensive approach needs to be adopted, that addresses all these issues in order to improve treatment compliance. Particular attention should be paid to factors within the health care system, such as access to services and the attitude and behaviour of health care providers as these lie within our sphere of influence.

10.1 Strategies for good adherence

In order to achieve good adherence to TB treatment the following steps must be followed at the start of TB treatment Adherence to treatment means following the recommended course of treatment by taking all the prescribed medications for the entire length of time necessary. Patients' adherence is a key factor in treatment success.

Promoting adherence through a patient centered approach that includes facilitating access to treatment, choosing with the patient the most convenient time and place for direct observation of treatment and, when possible, providing other social and medical services, is much more effective than spending resources on defaulter tracing.

Convenience to the patient must be balanced with the assurance of regular drug intake and monitoring, important to give the patient the best chances of cure. When patients receive self-administered treatment, they often take drugs irregularly, and tracing is difficult and often unproductive. In addition, there is a much longer period between interruption of treatment and initiation of treatment after tracing the patient. It is vital for health staff and community workers to offer polite and efficient attention, and to consider the patient's needs at every contact with the patient.

1) Getting to Know Your Patient

a) Obtaining Patient Information

For you to provide care that addresses the specific needs of your patients, it is important that you learn as much as possible about your patient's medical and social history, beliefs and attitudes about TB, sources of social support, potential barriers to treatment adherence, close contacts.

b) Assessing your patients' perceptions about TB

Understanding your patient's perspective is an important step toward ensuring adherence. However, the most important point to remember about assessing your patients' perceptions about TB is to first create an atmosphere of trust and acceptance so that your patients will feel comfortable discussing their thoughts with you.

The following questions may help you understand how your patients view their illness.

- What do you think causes TB?
- Why do you think you got sick when you did?
- What does TB do to your body?
- How severe do you feel your illness is?
- What treatment do you think you should receive for TB?
- What are the most important results you hope to receive from this treatment?
- What are the main problems your illness has caused for you?
- What do you fear about your illness?
- How do your family members or close friends feel about your TB?

Discuss openly and honestly any obvious differences in patient-provider perceptions. Correct patient misinformation.

Support discussions with objective information, such as chest radiographs or laboratory reports. Remember, when patients' perceptions are different from your own, you should acknowledge these differences. Accept that the patient has a different point of view and then make sure the patient understands your point of view about TB. You can make it clear that although you do not share your patients' views, you respect them.

Understanding your patients' perspective is an important step toward establishing a trusting relationship, which increases the likelihood of adherence.

Reasons why a person might not want to take TB medications.

- Undocumented immigrants and refugees may fear that having TB disease or infection will make them subject to legal action, such as deportation.
- Persons vulnerable to TB may have other life demands that are of higher priority to them than preventing or curing TB
- Mistrust in the public health system

- Some patients who use alcohol or drugs fear the side effects that may result from their taking TB medications while taking other substances
- Stigma associated with TB for many people may lead to shame, fear of social rejection, or fear of the loss of a job
- Attending a treatment centre for TB may mean taking time off work or other essential competing activities
- Some patients are afraid that TB drugs will cause dangerous side effects and lead to illness or extra medical costs
- Some people have strong cultural beliefs about health and treatment for disease that may compete with the prescribed regimen for TB

Ask patients about their concerns regarding TB

3) Assessing for Adherence

Health care workers often do not know that a patient is not following their recommendations. It is very important for you to determine whether your patients are taking medications as prescribed. Your first responsibility is to be aware of the general problem of non-adherence and to have a high index of suspicion. Consider several methods for assessing adherence.

i) Indirect Methods

Ask the patient whether he or she will be able or willing to take medications for the prescribed time. Ask for specific information:

- How often the patient takes medication
- The number of tablets taken
- How the patient remembers to take the medication
- Whether the patient has problems with the medications

Be sure to listen carefully and assure the patient that the information he or she tells you is very important.

- Monitor pills and appointments
- Check the patient's response to therapy by asking yourself:
- Has the patient's sputum result improved or converted to negative?
- Does the patient show general improvement?
- Have the TB symptoms improved or disappeared?

Address incorrect medicine taking by asking the following questions:

- Have you had any difficulty taking your pills?
- Over the past week, do you think you have taken your medicine as you should, on time and regularly?
- In general how often do you take the pills?
- In the past week, was there any time you missed taking your pills for more than one day?

b) Direct Methods

Directly observing your patient swallow each dose of medication is an effective method of ensuring adherence

4) Strategies for improving Adherence

a) In adults

Quality interaction with the patient:

- Create a partnership
- Ask patient whether they do take the TB drugs and do not assume that they do.
- Give each patient adequate time at each visit.
- Be positive do not intimidate or frighten the patient.
- Treat the person and not the disease.
- Understand and address different cultural beliefs and values.
- Adapt treatment to lifestyle.

- Make referrals to social welfare, where necessary.

Patient education:
- Give the vital information to the patient on diagnosis
- Be conscious and clear with instructions, as the patient might be anxious after hearing the diagnosis.
- Be clear about the duration of the treatment regimen.
- Do not overload the patient with too much information at the same time.
- Use educational materials that are culturally and linguistically appropriate for the patient.
- Assess the patient's beliefs about TB and if possible integrate the beliefs into the treatment plan.
- Review instructions, question patient to ensure understanding.
- Clarify patient's questions and respond clearly.
- Give written instructions.
- Describe specific adherence behaviours required.

During treatment:
- Modify the treatment plan to patient's suitability, offer options to the patient.
- Give clear instructions about medication side effects.
- Ensure proper record keeping for each patient on treatment.
- Follow up quickly on missed appointments.
- Fast track patients coming for treatment and follow up.
- Ensure that staff is supportive to patients
- Ensure that the physical environment is comfortable to patients
- Ensure confidentiality.
- Offer a holistic approach in addressing the patients' needs.

b) In children and adolescents

Children with TB present specific problems for adherence. However there is very little information about the rates of adherence among children or methods for addressing it. To improve adherence among children working with the parents or caregivers who will administer medications to the children is important. You cannot assume that parents will give the medication as prescribed, as some parents are non-adherent.

Provide anticipatory guidance:
- Talk with parents about the potential problems they might experience once treatment is initiated. For example, a child may resist taking medication, experience adverse reactions to the medication or have difficulty in swallowing medication.
- When parents are aware of potential problems they may be better equipped to deal with them and assist with the treatment.

Adolescents are at high risk of poor adherence because of concerns about stigma; they may not take their TB seriously; they may feel embarrassed about having to take TB treatment and concerned about what their friends think.

2) Educate and counsel the patient.

Patient education that is well planned and combined with other interventions is essential for ensuring adherence and it should be used in conjunction with other interventions. The goal of patient education is to influence or change patients' health behaviours by providing them with information that motivates them to follow the treatment plan to enhance each patient's care plan

This is an opportunity to provide information about the disease and treatment to the patient, identify potential problems that the patient may face during treatment and plan for optimal adherence. The following must be confirmed with the patient;

- Patient's residential and work physical addresses and contact details are correct
- Details of people that the patient has been in contact with in the past three months and stress the need for them to be screened for TB

Patient education plans should include information on several topics:

- Patient concerns about the disease, treatment, and follow-up care
- What causes TB
- How TB is transmitted
- Diagnostic tests and the meaning of the results
- Infection control measures
- Contact testing and evaluation
- The importance of following a healthy lifestyle
- Use simple, non-medical terms.
- Limit the amount of information you present in any one visit.

Adherence counselling must be structured in such a way that it includes the following aspects:

- Medication that the patient will be taking, when and how to take it, the side effects they may experience from the medication and what to do when the side effects develop.
- The duration of treatment; important milestones during treatment such as sputum testing to monitor the response to treatment and changes in medication; the importance of completing treatment
- Expected benefits of adherence
- Expected consequences of non-adherence
- Developing an adherence plan to identify barriers to treatment and address these to ensure treatment completion
- The link to HIV and the need for an HIV test
- General health issues including how to eat a balanced diet using readily available food, exercising, stopping smoking and reducing alcohol intake.

It is helpful for clinic staff or a community health worker to accompany the patient to their home. This allows verification of the patient's exact address. It provides an opportunity to arrange for screening of all household contacts, including other symptomatic household members and children under the age of 5 years and those who are HIV positive who require TB prophylaxis. It also presents an opportunity to identify social problems that could impact on adherence to treatment.

3) Develop a treatment plan for the patient

A clear treatment plan needs must be developed highlighting the important steps such as dates when sputa must be collected, medication changed and treatment completed. These dates should be clearly documented in the treatment section of the blue clinic card, the green patient-held card and the appointment diary as a reminder to both patients and staff. Advise the patient to inform clinic staff of any temporary or permanent change of address to facilitate continuation of treatment and of any movements over the treatment period to plan treatment during visits that may take place away from the area. If the patient unexpectedly travels away from the area advise to take the green card with them and to present it to the nearest clinic for treatment.

Social, economic, and health problems other than TB may hinder the patient's progress toward completing TB treatment. To minimise the effects of these problems on treatment, develop a problem solving strategy which should be included in this plan.

Provide clear instructions should on how to take the medication, possible side effects and what to do when they develop.

4) Patients' Rights

To ensure the realization of the right of access to health care services as guaranteed in the Constitution of the Republic of South Africa (Act No. 108 of 1996), the Department of Health is committed to upholding, promoting and protecting this right and therefore proclaims this PATIENT'S RIGHTS CHARTER as a common standard for achieving the realisation of this right:

- A healthy and safe environment
- Participation in decision-making
- Access to healthcare
- Knowledge of one's health, insurance/medical aid scheme
- Choice of health services
- Be treated by a named health care provider
- Confidentiality and privacy
- Informed consent
- Refusal of treatment
- Be referred for a second opinion
- Continuity of care
- Complain about health services

Responsibilities of the Patient

Every patient or client has the following responsibilities:

- To take care of his or her health
- To care for and protect the environment
- To respect the rights of other patients and health providers
- To utilise the health care system properly and not abuse it
- To know his or her local health services and what they offer
- To provide health care providers with the relevant and accurate information for diagnostic, treatment, rehabilitation or counselling purposes
- To advise the health care providers of his or her wishes with regard to his or her death
- To comply with the prescribed treatment or rehabilitation procedures
- To enquire about the related costs of treatment and/or rehabilitation and to arrange for payment
- To take care of health records in his or her possession

5) Directly observed treatment (DOT)

Directly observed treatment means that a treatment supporter watches the patient swallowing the tablets, in a way that is sensitive and supportive to the patient's needs. Close supervision and monitoring of patients ensures treatment compliance and early detection of adverse side effects due to medication.

The treatment supporter may be a health care worker or a trained workplace or community health worker, family member or whoever the patient chooses. The role of the treatment supporter is to motivate patients to continue treatment and to counter any factors that might result in treatment interruption.

The DOT services must be organised to suit the patient's circumstances and where possible treatment should be provided as close to home as possible. Patients who live close to a clinic may take their treatment at the clinic if convenient for them. There must be a fast tracking system for these patients and good infection control to minimise the risk of re-infection. The following must be conducted at each encounter with the patient:

1) Ask about side effects the patient may be experiencing and record in the patient card
2) Provide treatment for minor side effects
3) Refer patient to professional nurse or doctor if serious side effects
4) Give the patient their daily dose and observe intake

5) Record doses taken in patient-held green card and patient treatment record.
6) Update the TB patient diary to identify patients who did not present for DOT on that day and recall them rapidly.

7) Educate patient about treatment compliance

Medication for the weekend must be pre-packed for collection on Fridays and responsibility allocated to a family member to observe and sign the green card for doses taken on weekends.

Community DOT has the advantage of being more accessible and convenient to patients. A TB patient who has far to travel for treatment is less likely to adhere to treatment and community based DOT can be a viable alternative. In some areas, limited resources and high TB caseloads overwhelm clinics; using community-based DOT may contribute to a more rational use of limited resources in these settings. The treatment supporter can be a community health care worker or any community/ family member trained to provide DOT. Integration of this work within that of the PHC ward based outreach teams (WBOT) will allow for a sustainable community care programme. The community treatment supporters must be accountable to the facility manager.

6) Criteria for assigning treatment supporters

It is impossible to predict who will or will not take their treatment regularly, therefore appropriate support mechanisms should be put in place for the following patients. The following patients must be prioritised for treatment support;

- Children
- Elderly or infirm patients
- Patients with a history of interrupting treatment
- Patients with a history of substance or alcohol abuse
- Patients who are homeless or live under poor social conditions
- Patients with mental illness
- Patients who request a treatment supporter

Members of the patient's family should be encouraged to provide support and motivate the patient to complete treatment. At initiation of treatment, the family member or friend should be counselled together with the patient, so that they have all the information necessary to help the patient complete treatment. One of the difficulties with involving family is that underlying family dynamics can adversely influence treatment. Therefore when selecting a family member or friend to assist with treatment, it should be someone the patient trusts, respects and has a good mutual relationship with.

7) Engaging NGO/ CBOs in providing community TB care

The following must be considered where there are NGOs/ CBOs providing community care services;

a) Mapping of NGO'S providing community care services and determining how they might be able to contribute to community TB care
b) Involving community representatives in the selection of community treatment supporters and ensuring an appropriate geographic spread of treatment supporters.
c) Establishing a written contract with the community organisation and between the community organisation and the treatment supporter, defining roles and responsibilities and the standards required. The contracts should clarify whether incentives will be made available and under what terms.
d) Providing adequate training to CHW on TB: transmission, prevention, screening, diagnosis, treatment, side effects; monitoring response to treatment, HIV care, record-keeping; counselling.
e) Working with the community organisation to provide regular supervision, support, feedback and motivation of treatment supporters to ensure that quality outcomes are maintained.
f) Addressing ethics and confidentiality.

g) Establishing standard operating procedures and systems for:
   - Administering daily medication.
   - Monitoring adherence, including completion of the patient-held green card when doses are taken and methods for identifying those interrupting treatment.
   - Follow-up and recall of treatment interrupters.
   - Communication and feedback to clinic.
   - Reminding patients about sputa that are due during the course of treatment.

h) Record keeping at the clinic indicating the location of treatment supporters and patients allocated to them.

i) Providing regular feedback to the organisation on TB programme results and audits; addressing problems through joint problem-solving; acknowledging the community contribution to TB care.

8) The TB support team

In sharing responsibility for treatment outcomes, the roles and responsibilities of the TB support team need to be clarified. Building a good relationship between members of the team and the patient can help improve adherence. This can be achieved through:

- Creating a sense of partnership between the TB support team, the patient and their family
- Emphasising the importance of the patient (and family) taking responsibility for treatment, supported by health care personnel
- Giving the patient adequate time at each visit
- Treating patients with respect and consideration
- Being positive; not intimidating or frightening the patient
- Addressing any anxieties the patient may have
- Understanding the patient's cultural beliefs and values.

Table 10.2: Roles and Responsibilities of the TB treatment Support Team

TB Patient
• Take their tablets as prescribed • Report side-effects to the treatment supporter or clinic nurse • Return to the clinic for scheduled visits • Bring sputum specimens to the clinic for testing at the required times • Provide feedback to the team of any problems that they experience • Inform treatment supporter and clinic staff if they are going away and make plans for taking medication whilst away • Take responsibility for completing their treatment
Family / Friend:
• Provide emotional support to the patient • Encourage/remind patient to take their tablets daily • Supervise treatment on the weekends, or daily if required, and record doses in the patient-held green card • Remind patient to bring sputum specimens to the clinic for testing at the required times • Motivate patient to complete the full course of treatment • Report problems to the clinic
Nurse:

- Provide basic information on TB
- Initiate TB treatment and explain how to take the tablets
- In consultation with patient, allocate to DOT that is most suitable for them
- Provide daily treatment at the clinic for all patients for a minimum of 2-3 weeks and for those patients receiving Clinic DOT thereafter
- Keep a record of where all patients registered at the facility are receiving DOT
- Complete clinical records: clearly indicate when sputa are due; update records (blue clinic records)
- Update the TB register
- Assess patients on a scheduled basis, monitor response to treatment, encourage treatment completion
- Provide monthly treatment to the patient receiving DOT in the community or worklplace
- Get feedback from treatment supporters on patients receiving community DOT
- Arrange transfer of patients moving to another area
- Arrange tracing of patients who have defaulted treatment

Treatment supporter

- If possible, visit patients commencing treatment at their homes: assess and refer other suspects and contacts to the clinic; identify problems in the household that might affect adherence and report these to the clinic; confirm the patients address
- Meet with patients on a daily basis (including over weekends if possible) and supervise their treatment
- Complete the patient-held green card to record doses taken
- Ensure that patients have collected their monthly medication
- Provide support to TB patients and their families
- Motivate TB patients to complete their treatment
- Remind TB patients to bring their sputa to the clinic for testing at the appropriate times
- Provide regular feedback to the clinic on their patients
- Trace patients who have interrupted treatment
- Create awareness in the community about TB and HIV

Adherence Counsellor

- Provide structured education and counseling to patient
- Prepare patient for completing their TB treatment
- Assist the TB patient in anticipating problems with adherence and planning ways to overcome these
- Offer additional counseling to patients having problems with adherence

11. MANAGEMENT OF PATIENTS INTERRUPTING TREATMENT

Education, counselling and treatment support is the best way of avoiding treatment interruption. However, even with these measures in place there may be treatment interruptions that need to be addressed.

11.1 Minimising the duration of treatment interruption

When a patient doesn't keep a scheduled appointment for their treatment, the health care worker must enquire after the patient using the contact details provided and the appropriate means of tracing the patient. The next steps include;

- Finding out why the patient interrupted treatment
- Jointly developing an action plan to address the problems
- Re assessing the patient
- Initiation of treatment

Therefore early detection of patients who interrupt treatment and appropriate interventions is essential in preventing treatment default.

11.2 Managing treatment interruption

The management of patients who have interrupted treatment is complex and takes into consideration multiple variables including their immune status, degree of remission of the disease with the previous treatment and drug susceptibility. A simplified decision tree is suggested in the table below.

IF THE PATIENT INTERRUPTED TREATMENT FOR LESS THAN 1 MONTH
1) Trace the patient 2) Establish the cause for interruption of treatment 3) Address the problem or concerns/ counsel patient 4) Continue treatment and add the missed doses at the end of the treatment phase - If the interruption occurred during the intensive phase, the duration of this phase must be extended by the number of days that the patient did not take treatment. - If the interruption occurred during the continuation phase, the duration of this phase must be extended by the number of days that the patient did not take treatment.

IF PATIENT INTERRUPTS TREATMENT FOR 1 – 2 MONTHS			
ACTION 1		**ACTION 2**	
1) Trace the patient 2) Establish the cause for interruption of treatment 3) Address the problem or concerns/ Counsel patient 4) Collect sputum specimen for Xpert 5) Continue treatment and review results of the tests	If Xpert positive and Rif sensitive	• Continue treatment and add the missed doses at the end of the treatment phase	Monitor as usual until treatment is completed
	If Xpert positive and Rif resistant	• Stop treatment • Register patient as "RR-TB" • Refer to the MDR-TB treatment initiating site for further management	Follow up to ensure the patient has been successfully referred
IF PATIENT INTERRUPTED TREATMENT FOR TWO MONTHS OR MORE (LOST TO FOLLOW UP)			
1) Trace the patient 2) Establish the cause for interruption of treatment 3) Address the problem or concerns/ Counsel patient 4) Collect sputum specimen for Xpert 5) Do not start treatment, wait for the results	If Xpert positive and Rif sensitive	• Register as "Treatment after loss to follow up" • Restart Regimen 1	Monitor as usual until treatment is completed
	If Xpert positive and Rif resistant	• Register patient as "RR-TB" • Refer to the MDR-TB treatment initiation site for further management	Follow up to ensure the patient has been successfully referred

12. TB IN PREGNANCY

The prevalence of TB in pregnancy has increased exponentially since the onset of the HIV epidemic and ranks third as a cause for the overall maternal mortality after sepsis and hypertensive disorders. Seventy five percent of the TB cases were infected with HIV-1 and the relative risk of death was increased 3.2 fold in HIV-1 co-infection than non co-infected women.

Perinatal outcomes of infants born to women with tuberculosis were a significantly worse especially when the diagnosis is confirmed late in pregnancy and where adherence to treatment is poor. Occasionally, the diagnosis is only detected after the disease is confirmed in the newborn

12.1 Clinical features of tuberculosis in pregnant women

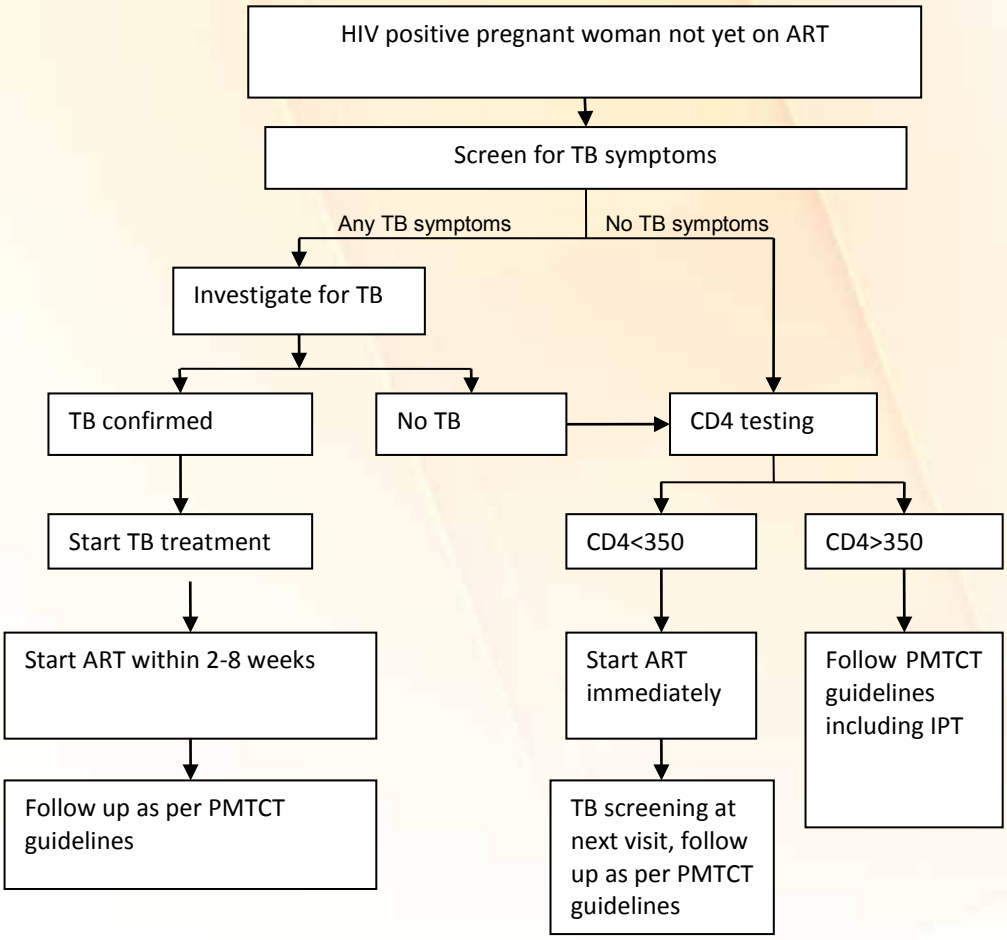
Pulmonary tuberculosis is the commonest presentation. Primary tuberculosis and extra pulmonary manifestations including miliary and meningeal disease in pregnancy are a particular risk factor for congenital tuberculosis. Mothers could develop infectious or non-infectious, drug-susceptible or drug-resistant tuberculosis either during pregnancy or during the postnatal period. Counselling of the pregnant women is essential to ensure adequate adherence.

All pregnant women should be screened for TB symptoms using the TB screening tool. Some women may be asymptomatic or may not present with a cough but other symptoms of TB such as loss of weight (or failure to gain weight in pregnancy), night sweats and fever. Therefore if any one of the symptoms is present, investigations for TB must be conducted. If a persistent cough is present sputum examination and a chest x-ray, if safe to do so, should be performed immediately. If extrapulmonary TB is suspected appropriate investigations based on the suspected site of disease may be conducted. The tuberculin skin test is unhelpful in adults.

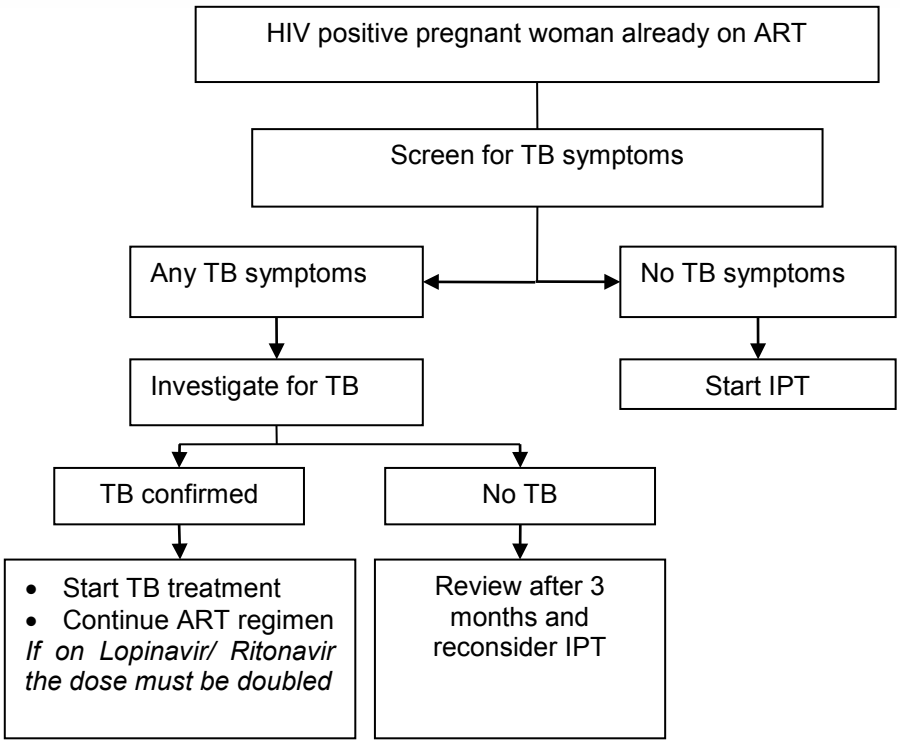
Women with confirmed tuberculosis during pregnancy without knowledge of their HIV status and the high risk pregnant women should be offered a HIV test with PICT.

For mothers where TB is suspected but not confirmed, post natal examination of placenta for calcification may also be useful. Where there is placental calcification, endometrial samples should be obtained within 72 hours of delivery and sent for mycobacterial culture and histological examination if possible.

TB screening algorithm for HIV-positive pregnant women not yet on ART



TB screening for HIV positive pregnant women on ART



Treatment

Untreated tuberculosis represents a far greater hazard to a pregnant woman and the foetus than treating the disease. Therapy must be commenced promptly with the standard daily 6 month treatment regimen. Most TB drugs except for streptomycin are safe for use in pregnant women. The first line drugs, isoniazid, rifampicin, ethambutol and pyrazinamide, are readily absorbed from the gastrointestinal tract and freely cross the placenta.

Adverse events

1) Risk of isoniazid-related hepatitis is 2.5 times higher in pregnant than in non-pregnant women
2) Various birth defects have been described with ethionamide and PAS while aminoglycosides are potentially ototoxic to the fetus.
3) Streptomycin is ototoxic to the foetus and should not be used in pregnancy.

12.2 Care of tuberculosis and HIV co-infection in pregnancy

Co-infection with HIV provides an indication for commencing ART regardless of CD4 count. Therefore patients diagnosed with TB before ART initiation must be started on TB treatment first and ART must be commenced within 2 – 8 weeks irrespective of the CD4 count.

In HIV positive pregnant woman who are on ART at the time of TB diagnosis, TB treatment should be commenced as soon as the diagnosis of tuberculosis is confirmed.

12.3 Breastfeeding women

Mothers must be encouraged to breastfeed their babies whilst on TB treatment. All the TB drugs are safe for use during breastfeeding. If the mother is infectious (both smear-positive and smear-negative/ culture positive PTB) surgical masks must be used to protect the child from infection.

12.4 Women taking hormonal contraceptives

Rifampicin may reduce the efficacy of the low dose combined oral contraceptive pill and may increase the risk of an unplanned pregnancy. A woman on oral contraception receiving rifampicin requires a high dose combined oral contraceptive, alternatively, another form of contraception should be considered.

There is no need to adjust the dose of injectable contraceptives (medroxyprogesterone acetate and norethisterone enanthate) in patients on rifampicin.

13. TB TREATMENT IN SPECIAL CIRCUMSTANCES

13.1 Liver disorders

Isoniazid, rifampicin and pyrazinamide are all associated with hepatitis. Of the three, rifampicin is least likely to cause hepatocellular damage, although the drug is associated with cholestatic jaundice; pyrazinamide is the most hepatotoxic.

Patients who are hepatitis virus carriers, have a past history of acute hepatitis or excessive alcohol consumption can receive the usual short-course chemotherapy regimen provided there is no clinical evidence of chronic liver disease. However, hepatotoxic reactions to TB drugs may be more common in these patients and should be anticipated.

13.2 Established chronic liver disease

High risk patients should have a baseline LFT conducted before initiation of TB treatment. If liver function is normal, the patient can safely continue with treatment and no further tests are necessary unless the patient develops symptoms of liver toxicity.

If the liver function test results are abnormal – elevated but less than 2x the upper limit of normal, the patient can be started on treatment but LFT's monitored monthly and patient assessed monthly for symptoms.

If the liver function tests are abnormal – enzymes elevated > 2x the upper limit of normal, the treatment must be stopped and patient referred to hospital for further investigation and management.

Patients with chronic liver disease should not receive pyrazinamide. Isoniazid and rifampicin plus one or two non-hepatoxic drugs such as streptomycin and ethambutol can be used for eight months. Alternative regimens are 9RE in the initial phase followed by 3HE in the continuation phase or 2 SHE in the initial phase followed by 10HE in the continuation phase, with a total treatment duration of 12 months. Therefore recommended regimens are 2SHRE/6HR, 9RE/3HE or 2SHE/10HE. Liver function should be monitored.

It is better to use rifampicin than isoniazid if necrosis is present or the liver pathology is undefined and isoniazid containing regimens if cholestasis is present.

13.3 Acute hepatitis

Uncommonly a patient has TB and concurrent acute hepatitis (e.g. acute viral hepatitis) unrelated to TB or TB treatment. Clinical judgment is necessary in making treatment decisions. In some cases it is possible to defer TB treatment until the acute hepatitis has resolved. In cases where it is necessary to treat TB during acute hepatitis, the combination of SE for the first 3 months is the safest option. If the hepatitis has resolved, the patient can then be given isoniazid and rifampicin during the continuation phase for six months. If the hepatitis has not resolved, SE should be continued for a total of 12 months. The treatment alternatives are therefore 3SE/6HR or 12SE.

13.4 Renal failure

Isoniazid, rifampicin and pyrazinamide are either eliminated almost entirely by biliary excretion or metabolized into non-toxic compounds. These drugs can therefore be given in normal dosages to patients with renal failure. In severe renal failure, patients should receive pyridoxine with isoniazid in order to prevent peripheral neuropathy. Streptomycin and ethambutol are both excreted by the kidney. Where facilities are available to monitor renal function closely it may be possible to give streptomycin and ethambutol in reduced doses. The safest regimen to be administered in patients with renal failure is 2HRZ/4HR.

13.5 Tobacco smokers

The interventions for tobacco dependence include;

- brief routine advice to stop smoking
- intensive support to quit
- pharmacological treatment

The combination of interventions depends on the patient's needs. At primary health care level, brief routine advice and some pharmacological treatment can be offered routinely by nurses or doctors.

1) *Brief routine advice*

Every TB patient should be asked if he or she smokes and those who smoke should be advised to quit. Assistance should be provided to those who smoke and are interested in quitting. Patients who are not ready to quit should be educated about the dangers of smoking and asked to consider the possibility and seek help in the future. The "Five A's Approach" is recommended, it consists of five steps and takes 5-10 minutes to implement.

STEP 1: ASK if the patient smokes tobacco	**Identification of smokers among new TB patients.** 1) Every patient should be asked about tobacco use - If smoking, how often (daily, occasional) - If not smoking, have they ever smoked - If former smoker, why did they stop 2) Record this is the Patient Treatment record (GW 20/12)
STEP 2: ADVISE the patient to quit	**Discouraging smoking among TB patients** 1) Every TB patient who smokes should be offered counseling. 2) Every TB patient who smokes should also be educated about the dangers of smoking to themselves and to others.
STEP 3: ASSESS the patients willingness to quit	1) Ever TB patient who smokes should be asked about their willingness to stop smoking. - Review reasons for quitting - Establish whether the patient is able to quit - Address patients concerns 2) If the patient is willing to quit within the next month, proceed to STEP 4. 3) For patients unwilling to quit tobacco use following counseling, strongly advise them to stop smoking. - Address the patient's concerns and fears - Consider counseling approach in Table 13.2 , below
STEP 4: ASSIST the patient to quit	1) Motivate patient to quit smoking at every encounter; - provide advice on stopping - explain the benefits of stopping smoking - agree on a quit date - provide treatment

STEP 5: ARRANGE for follow up	1) Assess patients progress monthly - Motivate the patient - Provide the necessary psycho social support to the patient - If tobacco use has occurred, review the reasons for this, counsel the patient and continue with abstinence.

Table 13.2: COUNSELING APPROACH FOR TB PATIENTS WHO ARE UNWILLING TO QUIT SMOKING

RELEVANCE	1) Encourage the patient by stressing the benefits of quitting - Improving chances of getting cured - preventing death as a result of TB - preventing spread of TB infection at home 2) Quitting is even more important when the patient is a pregnant woman or has other conditions such as HIV infection, diabetes, asthma, chronic bronchitis, COPD or silicosis.
RISKS	1) Explain the risks of continuing smoking to the patient - risk of relapse after treatment completion - risk of TB disease among the household contacts due to passive smoking - harm to the unborn baby for pregnant women - increased susceptibility to respiratory infections for a HIV positive patient - cardiovascular complications of diabetes, - exacerbation of asthma, chronic bronchitis, COPD or silicosis. - risk of heart attacks, strokes, lung and other cancers, respiratory impairment in the long term.
REWARDS	1) Ask the patient about how his non medical benefits of stopping smoking. Note the most relevant ones, such as: - Feeling better about oneself - Performing better in physical activities - Saving money for better use - Being exemplary to children - Protecting family members
ROADBLOCKS	1) Ask the patient about obstacles to quitting, these could include; - Withdrawal symptoms - Fear of failure - Weight gain - Depression and missing the enjoyment of tobacco
REPETITION	1) The motivational counselling should be conducted at least once a month for patients who remain unmotivated to quit smoking

2) *Intensive support to quit*

Where feasible, group counseling sessions on smoking cessation facilitated by trained health care workers may be conducted. Patients with nicotine addiction or co-morbidities must be referred for intensive behavioural interventions.

3) *Pharmacological treatment*

Many patients successfully quit smoking with counseling, others cannot and could benefit from pharmacotherapy. Pharmacotherapy may be considered in TB patients with withdrawal symptoms but for optimal effectiveness, drug therapy always requires counseling and behavioral support. There are two types of pharmacotherapy;

- ***Nicotine replacement therapy:*** this refers to medication containing nicotine that is intended to partially replace the nicotine formerly obtained from tobacco. It reduces general withdrawal symptoms and provides some effects for which the patient previously relied on smoking such as handling stressful or boring situations. It can be discontinued within three months after smoking cessation. Available delivery systems include transdermal patches, chewing gum, lozenges, sublingual tablet, nasal spray.

- **Non-nicotine medications:** The non-nicotine medications are indicated in patients who
  - are unable to tolerate nicotine replacement products
  - who have failed nicotine replacement therapy
  - who do not want to use nicotine replacement products.

The medicines used include clonidine, bupropion hydrochloride and nortriptyline, which must be prescribed by an experienced health care professional.

13.5 Excessive alcohol use

TB patients must be asked about history of or current alcohol use. The Alcohol Use Disorders Identification Test (AUDIT) will help identify people with hazardous/ risky drinking, harmful drinking and alcohol dependence. As alcohol-use disorders can cause the deterioration of living conditions and impact negatively on TB treatment outcomes, appropriate measures should be routinely offered to those screened positive for harmful drinking and alcohol dependence. The appropriate interventions based on the AUDIT scores are summarized in the table below.

Scores	Category	Intervention	
0 – 7	Low risk	Alcohol education	1) Inform the patient about the screening results 2) Identify risks and discuss consequences 3) Provide medical advice 4) Solicit patient commitment to reducing/ stopping alcohol use 5) Identify goal (reduced drinking or abstinence) 6) Give advice and encouragement 7) Provide educational materials
8 – 15	Excessive	Simple advise and patient education	
16 – 19	Harmful and hazardous drinking	Simple advise, brief counselling and continued monitoring	
20 - 40	Alcohol dependence	Referral to specialist for evaluation and treatment	

13.6 Diabetic patients

Treatment is the same as for all other patients. If patient has diabetic nephropathy the doses of Pyrazinamide and Ethambutol may have to be adjusted. TB treatment may be extended to nine months in patients who have severe TB disease. Pyridoxine (10-25mg/day) should be added to the treatment in order to prevent INH induced neuropathy as diabetic patients are at higher risk of developing peripheral neuropathy. Monthly blood glucose monitoring must be conducted during TB treatment . Ensure optimal glycaemic control by ensuring compliance to treatment and education of the patient about lifestyle changes – diet, physical activity.

13.7 Silicosis

There is no specific treatment for silicosis based on current evidence. The management TB patients with silicosis require early diagnosis of both diseases. Silicosis has typical chest x-ray changes, awareness of the radiological presentations is important for early diagnosis. TB treatment is the same as for all other patients. Symptomatic treatment should be added if the patient presents with signs of COPD. Silica and Silico-tuberculosis in exposed workers is a compensable disease according to the Occupational Diseases

in Mines and Works Act, 1973. The Act covers mine and quarry workers diagnosed with pulmonary TB whilst in employment or within 12 months of leaving such employment. If the patient has pre existing silicosis, the claim can be submitted irrespective of when the patient left employment. Such claims should be submitted to the Medical Bureau of Occupational Diseases.

14. TB AND HIV

HIV infection leads to progressive immunodeficiency and increased susceptibility to infections, including TB. As HIV infection progresses, CD4 lymphocytes decline in number and function. The immune system is less able to prevent the growth and local spread of Mycobacterium tuberculosis, leading to the progression of recent or latent TB infection to active TB disease.

HIV not only increases the number of TB cases but also alters the clinical course of TB disease. Although tuberculosis can occur at any point in the course of progression of HIV infection, the clinical pattern of disease changes. As HIV related immune suppression increases, there are increasing numbers of smear-negative pulmonary TB, extra-pulmonary TB and disseminated TB cases. TB is also more difficult to diagnose as immunosuppression progresses. Co-infected patients have an increased mortality due to rapid disease progression, late diagnosis and other opportunistic infections.

Appropriate TB case management including the provision of comprehensive HIV care to the co-infected patient will l prolong the lives of people living with HIV and AIDS, minimize the negative effects of TB on the course of HIV and interrupt the transmission of M. tuberculosis.

14.1 Diagnosis of HIV in TB patients

The definitive diagnosis of HIV infection rests on a positive HIV test. All confirmed TB patients must be offered HIV counselling and testing. In children under 12 years of age, parents or the legal guardian of the child should be counselled and asked to provide consent for the test. Ideally, the offer of an HIV test should take place during the diagnostic work-up for TB or soon after the initiation of TB treatment. The benefits of knowing the HIV status include:

- Early diagnosis and management of other HIV-related illnesses.
- Opportunities for prevention of other infections (e.g. using cotrimoxazole).
- Access to ART
- Access to HIV care (psychosocial, nutritional, medical)
- Decreased HIV transmission and re-infection through condom use.

14.2 Package of care for co-infected TB patients

Appropriate HIV-care of co-infected patients is essential to help reduce their morbidity and mortality. Whilst an HIV positive patient is on TB treatment, it is the responsibility of the TB staff to ensure that the patient is provided with or accesses appropriate HIV care. Where possible, these services should be provided to the patient at the same clinical visits for TB. All HIV positive patients require a baseline HIV assessment soon after confirmation of diagnosis to help determine the extent of progression of their HIV and their HV treatment plan.

Components of HIV care to be provided to TB and HIV co-infected patients include:

- Immunological staging with CD4 counts: The CD4 count assesses the number of T-helper immune cells in the blood and is an indication of the level of immunosuppression.
- An RPR test to screen for syphilis.
- PAP smears for all HIV positive women.
- Symptomatic screening for STI's at every visit and syndromic management of STI's.
- Reproductive health-care with an emphasis on effective contraception whilst on TB treatment and the use of condoms to prevent transmission of HIV and to avoid re-infection.

- Cotrimoxazole prophylaxis against opportunistic infections.
- Diagnosis and management of other opportunistic infections.
- Nutritional assessment and the provision of nutritional supplements.
- A social assessment including:
  - Family circumstances and the status of caregivers.
  - Identification of orphans or vulnerable children.
  - Applications for disability grants, child support grants or care dependency grants.
- On-going counseling support
  - To assess how the patient is dealing with their HIV status.
  - To discuss disclosure and support available to the patient.
  - To emphasise messages about practising safer sex to reduce re-infection and prevent transmission
  - To reinforce good adherence to treatment.
  - To re-assure and encourage patients
- Fast tracking ART initiation

Integration of care provided to co-infected patients preferably by one service provider will ensure comprehensive management of the patient, reduce morbidity and mortality and improve treatment outcomes.

14.3 Cotrimoxazole prophylaxis

Prophylaxis against inter-current infections decreases morbidity and mortality in HIV positive TB patients. Cotrimoxazole prophylaxis is highly effective in preventing pneumocystis carinii pneumonia, toxoplasmosis, isosporiasis and other bacterial pneumonias. Cotrimoxazole prophylaxis has been shown to be effective while the patient is taking it, so it should be taken lifelong. However in patients on ART, CPT can be stopped once the CD4 is >200. CPT has also been shown to decrease hospitalisation and mortality in HIV infected TB patients. As a result CPT is recommended as part of a minimum package of care for HIV positive adults and children.

Cotrimoxazole must be given daily to all HIV positive TB patients, unless it is contra indicated. This must be introduced within a month of starting TB treatment, to help differentiate between side effects that may develop. Before initiation of CPT, patients must be counselled on its effectiveness, side effects and the importance of adherence. Recommended dose: Cotrimoxazole 960mg (2 single strength tablets or 1 double strength tablet) daily. Side effects of co-trimoxazole include; maculopapular rash, hepatitis, neutropaenia and other haematological abnormalities.

14.4 Antiretroviral therapy and TB

Co-infected TB patients irrespective of CD4 count require antiretroviral therapy (ART). The ART initiation is determined by whether the patient develops TB whilst on ART or presents with TB before commencing ART. Four issues complicate the management of a patient on TB treatment and ART:

- The interaction of rifampicin with NNRTIs and PIs.
- Increased drug toxicity.
- Increased pill burden and the impact on adherence.
- Paradoxical tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS)

1) *Drug interactions*

Rifampicin induces the cytochrome P450 liver enzyme that metabolizes PIs and NNRTIs. This can lead to a reduction in the blood levels of PIs and NNRTIs. The reductions in levels are greater for PIs than for NNRTIs and greater for nevirapine than efavirenz. These drug interactions may result in ineffectiveness of antiretroviral drugs and potential development of HIV drug resistance, particularly if lopinavir/ ritonavir is used with rifampicin-based TB treatment without an adjustment in dose of the lopinavir/ ritonavir. Efavirenz at standard doses can be used with standard TB treatment, as the reduction in efavirenz levels caused by rifampicin does not affect virological suppression.

2) Side effects

Table 1: Shared Side Effects of TB and Antiretroviral Therapy

Side effects	Antiretroviral treatment	Tuberculosis treatment
Nausea and vomiting	Didanosine, zidovudine, protease inhibitors	Pyrazinamide
Hepatitis	Nevirapine, efavirenz Protease inhibitors (especially when dose is increased to overcome rifampicin induction)	Rifampicin, isoniazid, pyrazinamide
Peripheral neuropathy	Stavudine, didanosine	Isoniazid
Neuropsychiatric side effects	Efavirenz	Isoniazid
Renal toxicity	Tenofovir	Rifampicin
Rash	Nevirapine, efavirenz	Rifampicin, isoniazid, pyrazinamide, ethambutol streptomycin

Initiation of ART in TB patients

Table : Antiretroviral Treatment for Adults with Concomitant TB

TB develops while on ART	TB diagnosed before starting ART
ART should be continued throughout TB treatment, with changes to the regimen as follows: **If on First-line regimen.** 1) In patients on efavirenz-containing ART, continue the same ART regimen and start TB treatment. 2) In patients who are stable on nevirapine-containing ART - start TB treatment - switching to efavirenz is not necessary - regular ALT monitoring needs to be undertaken. **If on Second-line regimen** 1) Adjust ART regimen as follows; - Lopinavir / ritonavir 400/100mg every 12 hours should change to lopinavir / ritonavir 800/200 mg every 12 hours - This should be continued until 2 weeks after completion of TB treatment, when the dose can be reduced to the standard dose. 2) Monitor ALT monthly during TB treatment.	**Patients with a CD4 count <50:** Fast track - start ART within 2 weeks after starting TB treatment **Patients with a CD4 count >50:** Start ART within 2 – 8 weeks after starting TB treatment **Patients with TB meningitis (irrespective of CD4 count:** Defer ART until 8 weeks after starting TB treatment

ON COMPLETION OF TB TREATMENT ALL CO-INFECTED TB PATIENTS MUST BE ON ART

3) *Paradoxical TB-Immune reconstitution inflammatory syndrome (TB-IRIS)*

About 20% of HIV-infected patients who start ART while on TB treatment will develop paradoxical TB-IRIS. These patients have typically had improvement of their TB symptoms on TB treatment but then experience a recurrence of TB symptoms or new symptoms and signs of TB in the first few weeks after starting ART. The underlying mechanism is thought to be that the recovering immune system on ART drives inflammatory reactions to TB antigens still present at the sites of TB disease.

Risk factors include low CD4 count, disseminated TB and short duration between TB treatment and ART. Paradoxical TB-IRIS is infrequently fatal and ART should not be delayed in patients with low CD4 counts in order to prevent TB-IRIS, as the mortality associated with delaying ART is high.

Common clinical features include enlarging lymph nodes, fevers, worsening chest radiograph infiltrates and enlarging pleural effusions. When TB-IRIS results in meningitis or enlarging tuberculomas this may be life-threatening.

An immune reconstitution illness is not indicative of drug failure or a drug side effect.

ART should not be stopped, if a life-threatening immune reconstitution develops, the patient must be referred to the hospital. In any patient presenting with paradoxical TB-IRIS it is very important to exclude MDR TB and other causes (such as bacterial pneumonia) that may account for the clinical deterioration, as the diagnosis of paradoxical TB-IRIS is a diagnosis of exclusion.

Prednisone is indicated in patients with severe symptoms and the recommended dose is;
Prednisone 1-2 mg for 4 weeks and taper over two weeks

4) *Counselling of co-infected patients*

Patients on TB medication and ART must be counselled on both TB and HIV to improve adherence to both treatment regimens. This should include adherence counselling covering specific problems they are likely to encounter during treatment:

- large number of tablets to be taken daily
- worsening of TB symptoms as part of IRIS when antiretroviral treatment is commenced.
- side effects of all the medicines and what to do when they experience them
- possible interactions between TB and ARV medicines

15. DRUG RESISTANT TUBERCULOSIS

In 2001 the estimated prevalence of MDR among new cases was 1.8% and 6.7% among previously treated cases . The estimated number of new MDR-TB cases annually was 8 000. The emergence of XDR-TB in 2006 and subsequent surveillance has shown a prevalence of 9% among MDR-TB patients. Several molecular epidemiological studies have confirmed ongoing transmission of drug-resistant tuberculosis. Nosocomial outbreaks of MDR-TB associated with HIV infection have been documented where HIV positive patients being treated in hospitals for drug susceptible tuberculosis have been re-infected with MDR strains. Studies have shown that patients with active, untreated MDR-TB can infect large numbers of HIV positive individuals, leading to significant outbreaks of MDR-TB with high case-fatality rates. Prevention is the key to effective MDR-TB control.

15.1 Factors contributing to MDR-TB

As with other forms of drug resistance, MDR tuberculosis is a man-made problem, being largely the consequence of human error in any, or all of the following:

1) Management of drug supply.

2) Patient management, including prescription errors.
   - Poor relationships between patients and health care personnel due to the uncaring staff attitudes, showing little empathy for patients, being paternalistic and failing to adopt a problem solving approach to help resolve issues all contribute to poor adherence.
   - Inadequate counselling of patients resulting in low knowledge levels, poor understanding of what is expected of them and of the importance of completing treatment and monitoring the response to treatment also contribute to poor adherence to first line regimens.
   - Ineffective systems, including lack of support for directly observed therapy and unsupervised patients; poor record keeping, follow-up of patients and referral.
   - Staffing issues including frequent staff changes, poor staff morale, lack of regular support and supervision and low accountability of staff for programme outcomes.
   - Insufficient contact tracing and follow-up of MDR cases also contributes to the spread of MDR-TB.

3) Patient adherence is most often a problem when;
   - The patient is homeless, has an alcohol or drug problem, and is unemployed and/or looking for a job.
   - A family member has been unsuccessfully treated previously.
   - Access to health care is difficult.

15.2 Definitions of drug resistant TB patient categories

Patients with drug resistant TB are categorised by the resistance pattern of MTB strains isolated in their sputum or other specimen.

Rifampicin Resistant TB (RR-TB)	Resistance to rifampicin, with or without resistance to other TB medicines. This maybe mono, poly, multi or extensive drug resistance.
Multi Drug Resistant TB (MDR-TB)	Resistance to at least both rifampicin and isoniazid
Extensive Drug Resistant TB	Resistance to any fluoroquinolone and to at least one of the three second line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multi drug resistance.
Mono resistance	Resistance to one of the first line TB medicines (rifampicin, isoniazid, pyrazinamide or ethambutol)
Poly Drug Resistant TB	Resistance to more than one first line TB medicines. This excludes resistance to both rifampicin and isoniazid.

15.3 Early diagnosis and management of MDR-TB

The introduction of rapid diagnostic tools for RR-TB and MDR-TB has drastically reduced the time to diagnosis. It is important to always evaluate the clinical condition of the patient and not rely solely on a laboratory result, because there could be errors due to administrative factors or contamination of the sample. If a laboratory result is not consistent with the clinical picture, the test should be repeated.

- **All RR-TB patients must be reported by the NHLS to the requesting facility within 24 hours of diagnosis and to the district, provincial and national TB managers weekly.**
- **Diagnosed RR-TB patients must be started on treatment within 5 days from date of sputum specimen collection for testing.**

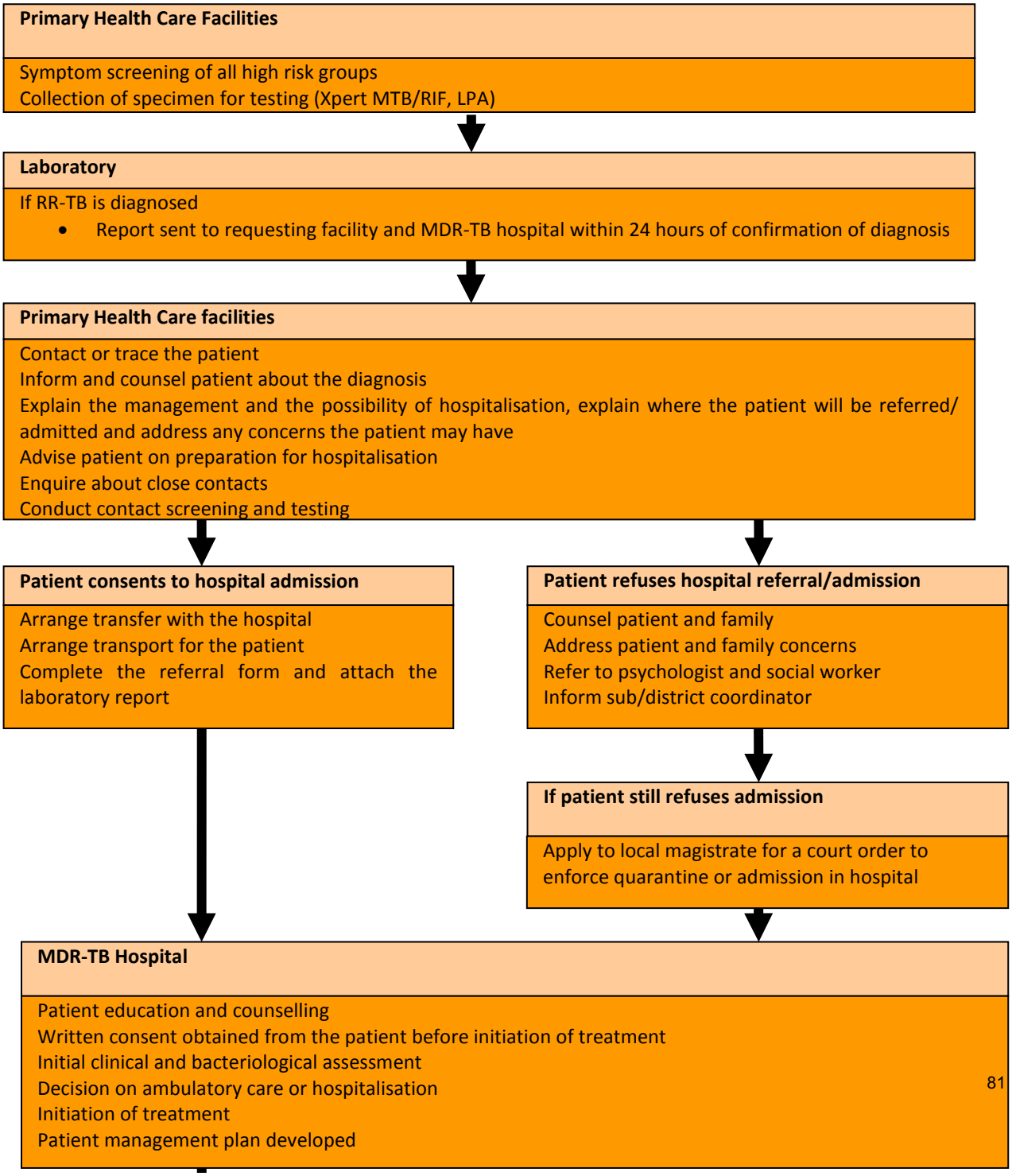
15.4 Treatment for drug resistant TB

Types of resistance	Treatment
Isoniazid mono resistant TB	RHZE for 6 – 9 months
Any Rifampicin resistant TB	MDR-TB regimen for 18 – 24 months

Management of MDR-TB at all levels should include:

- Rapid testing using Xpert MTB/RIF
- Confirmatory DST for patients with RR-TB
- Rapid tracing and linkage to treatment
- Rapid tracing and evaluation of contacts.
- Standardised MDR-TB treatment in MDR-TB treatment initiation sites
- Hospitalisation of patients until they are confirmed to be non infectious
- Outpatient management of patients who meet the set criteria
- Provision of appropriate adherence counselling and treatment support
- Ensuring continuum of treatment and care during treatment
- Monitoring treatment compliance
- Implementing measures for rapid recall if patients interrupt their treatment
- Good clinical records keeping and updated registers
- Ongoing education and motivation of patients
- Provision of psycho social support
- Early identification, management and reporting of adverse events

Figure 15: Patient flow algorithm



The Role of Primary Health Care (PHC) facilities in the management of MDR-TB:

Although the DR – TB treatment initiation sites have the key responsibility for the treatment of MDR-TB, primary health care facilities have an important role to play in:

- Ensuring early diagnosis of DR-TB in patients
- Refer all confirmed DR-TB patients for treatment immediately
- Conducting screening and testing of all DR-TB contacts.
- Providing on-going care post discharge from the MDR-TB treatment initiation sites
- Providing counselling and support to patients with DR-TB, their families and contacts.

On discharge from MDR hospital, patients will continue treatment at the PHC facility and be evaluated monthly by the MDR unit.

- mechanisms for feedback on patient follow up and adherence monitoring should be established between the MDR unit and PHC facility prior to discharge.
- the PHC facility should receive MDR drugs from the MDR hospital on a patient name basis and provide these to the patient through clinic DOT or home based care.
- Adequate records of individual patient progress as well as hospital registers are required to monitor overall response to treatment and track treatment outcomes.

15.5 Managing patients who refuse treatment

Treatment is voluntary, adequate counselling should be provided to the patient to ensure they understand the implications of not taking the treatment on their health and that of others. Full knowledge regarding the treatment must be communicated for them to make an informed decision. For MDR and XDR-TB treatment informed consent must be obtained from the patient or family member or designated person in cases where the patient is not in a state to make a decision. Where all efforts fail to convince patient to take treatment, the facility manager may approach the local Magistrates office to obtain a court order to enforce hospitalisation where the patient is a public health risk to other people. When a patient terminates consent for treatment, the patient must sign the Refusal of Treatment form.

15.6 MDR-TB Contact Management

Prompt contact tracing should be conducted for all RR-TB patients:

a) If symptomatic: the contacts should be appropriately investigated, using Xpert or LPA to determine whether they have RR-TB or MDR-TB. It is recommended that symptomatic children be referred to the hospital for evaluation, as MDR-TB diagnosis is more difficult in children than in adults.

b) All asymptomatic close contacts of MDR-TB patients should be screened at six monthly intervals for up to two years. HIV positive contacts should be followed-up 3 monthly and if active MDR-TB develops, referred immediately for treatment. Asymptomatic patients should also be educated about the signs and symptoms of TB and informed to present at a health facility immediately if these develop.

15.7 TB preventive therapy for asymptomatic contacts of MDR patients

Asymptomatic child contacts of smear or culture positive MDR-TB should be managed according to the standard recommendations for drug susceptible TB. **Child contacts under 5-years of age** should be given INH preventive therapy, irrespective of tuberculin response. **HIV-infected children of any age** should be given INH preventive therapy, irrespective of tuberculin response.

15.8 Treating Mono and Poly-Resistance

Patients with mono and poly-resistance must be referred to the MDR-TB hospital for assessment and initiation of treatment but should not be admitted in the hospital. The PHC facility must then monitor the patient throughout the treatment period and the treatment outcomes must be reported to the MDR-TB Treatment initiation site. Where DR-TB registers are kept at PHC level, these patients must be registered in these registers and the data collated at district level.

15.9 XDR-TB

XDR-TB is extremely difficult and expensive to treat. It has very high mortality, with rates of over 90% recorded amongst HIV co-infected XDR patients in Tugela Ferry, KwaZulu-Natal. Prevention is key to the control of XDR- TB. Just as good case management of new and retreatment cases will prevent MDR-TB, good case management of MDR-TB will prevent XDR-TB. There is probably no difference in the spread of XDR-TB to any other form of TB.

On confirmation of MDR-TB the laboratory should conduct second-line DST routinely.

By the time confirmation of XDR-TB is made these patients would ideally be on MDR-TB treatment. However, XDR-TB requires an individualised approach to treatment regimes, based on the previous history of drug use and the results of drug susceptibility testing. The duration of stay in the hospital may vary from patient to patient depending on the clinical response to treatment, on average it is six months. On discharge these patients are followed up at the clinic or at home with monthly assessments conducted at the MDR-TB site.

16. ADMISSION AND DISCHARGE CRITERIA FOR TB PATIENTS

Hospital care for DS-TB patients is indicated in some circumstances, and specific admission and discharge criteria help to optimise care for all TB patients. TB patients are only admitted to hospital care when either their clinical condition warrants it and / or access to community-based care is not available. It is equally important that TB patients be discharged to outpatient care at clinics as soon as they can be managed effectively in the community. TB hospitals only admit patients with active TB who meet specific criteria and referred from hospitals or clinics. In areas where there are no TB hospitals, the same criteria apply to the TB wards in general hospitals.

16.1 Admission criteria to TB hospitals

a) Referrals from clinics/ CHC to TB hospitals are indicated if at least one of the following admission criteria are met:
   - A medical reason for admission - when patients diagnosed with TB are too ill or too weak to go home, including severely emaciated TB patients without other complications.
   - Social or socio-medical reasons for admission - when clinic or community support and care cannot be achieved, particularly in patients with alcohol or drug dependence, mentally illness or previously non-compliant patients.
   - Patients medically stable (no acute illness)

In all cases, a TB referral form should be completed. This form must include relevant basic personal, clinical and diagnostic information e.g. confirmed sputum smear or culture results or other reasons for making the diagnosis of TB and treatment that the patient is taking.

b) Admission of patients from general hospitals to TB hospitals should only take place when the TB diagnosis has been confirmed and the patient's other medical conditions have been stabilised:
   - Patients with negative smears require a culture to confirm PTB.
   - Other conditions such as bacterial or viral pneumonias, congestive cardiac failure, asthma, chronic obstructive lung disease, bronchiectasis and bronchial carcinoma need to be excluded in the differential diagnosis.
   - TB patients with medical conditions such as diabetes mellitus, epilepsy and severe hypertension should be stabilized before referral.
   - Severely ill patients with extra-pulmonary TB (TB meningitis, TB spine, TB pericarditis) need to be stabilised in general hospitals before transfer to TB hospitals.

16.2 Essential elements of in-patient care in TB hospitals

1) Clinical management
   - Appropriate treatment
   - PICT
   - CD4 count and baseline tests for HIV positive TB patients
   - Staging
   - ART initiation
   - Early identification and treatment of adverse event

2) A health education plan should be implemented within one week of admission to counsel the patient about TB and to develop an adherence plan to ensure treatment completion.

3) Psycho-social evaluation and support.

4) Within two weeks of hospitalisation, a plan for continuum of care on discharge should be developed:
   - Confirm the patient's correct address
   - Contact the local clinic and organisation providing community TB care to link the patient to care.
   - Contact or meet with family members to discuss the treatment plan and to ensure treatment support when the patient is discharged.

It is the responsibility of the TB hospital to offer all co-infected patients the full package of HIV care. Once they are clinically ready for discharge, referral forms must be completed to ensure continuum of care.

16.3 Criteria for referral from TB hospitals to district / regional hospitals

Patients should be referred to a secondary or tertiary hospital if their clinical condition warrants more specialised care than the TB hospital can provide. This includes:
- All severe complications of TB disease e.g. massive haemoptysis, TB meningitis
- Severe dyspnoea and empyema.
- Severe drug reactions e.g. acute liver failure, Steven Johnson syndrome.
- HIV related diseases that need specialised medical care e.g. cryptococcal meningitis.

16.4 Discharge criteria from TB hospitals to PHC clinics

TB patients should be discharged from TB hospitals to PHC clinics as soon as the following two criteria are met:
- The patient is medically stable (no dyspnoea, no haemoptysis, not severely emaciated and afebrile) and able to care for him/herself (or adequate family or community-based care is arranged).
- The patient is able to access treatment at a clinic and be monitored either at the clinic or community.

16.5 Discharge process

1) Within 2 weeks of admission a discharge plan must be completed which ensures:
   - Continuation of care (contact with the most accessible clinic, assigning a treatment supporter)
   - The patient knows about their TB management (how and when to take medication; duration of treatment; importance of compliance with the treatment; attendance at the nearest clinic for clinical evaluation and provision of sputa to monitor response to treatment; infection control measures to be taken at home).
   - A formal link is established between the patient, the local clinic and treatment supporter.

2) Psycho-social support – a social worker needs to be involved to arrange the appropriate social support for patients in need.

3) Completing the referral form in detail with all the relevant information.
   - One copy is for the patient to take to the clinic; one copy should be sent to the referral clinic; one is kept at the hospital.
   - The green patient card should be updated before the patient leaves the TB hospital and the clinic or DOT supporter should keep it updated until the TB treatment is completed.

17. TB IN HEALTH CARE WORKERS

People with undiagnosed, untreated and potentially contagious TB are frequently seen in health care settings. In an era of increased access to HIV services such as Voluntary Counselling and Testing, Prevention of Mother to Child Transmission and Antiretroviral Therapy, increasing numbers of HIV positive patients are also seen in these facilities. HIV positive patients are particularly vulnerable to TB with a 10% annual risk of developing TB compared to a 10% lifetime risk in those with normal immunity. It is estimated too, that 10% of those newly diagnosed with HIV have undiagnosed TB; half of these are infectious. The increasing numbers of undiagnosed TB, TB suspects, TB patients and immunocompromised patients all present in the same environment create the potential for high levels of nosocomial transmission of TB.

An increased risk of TB has been documented amongst all categories of health care personnel (including facility staff, community health workers and volunteers) compared to the general population. The prevalence of HIV amongst health care personnel correlates with that in the general population. Health care personnel are at risk due both to frequent exposure to patients with infectious TB and because they may also be immunocompromised due to HIV.

It is the responsibility of management and staff to minimise the risk of TB transmission in health settings. Infection control measures should be established to reduce the risk of TB transmission to both the general population and to health care personnel. Since the majority of patients are seen at primary health care level, it is important to ensure that measures to prevent the spread of infection focus not only on hospitals, but are implemented also at primary health care level.

17.1 Protection of health care personnel

All categories of health care personnel have an increased risk of TB when compared to the general population. In addition to reducing their exposure, specific measures that target health care personnel are required:

- Informing health care personnel of the signs and symptoms of TB and encouraging early recognition of symptoms and presentation for sputum tests
- Ensure that all health care personnel with signs and symptoms are evaluated as “high risk TB suspects” and have 2 sputum specimens sent for evaluation: a spot specimen for smear and an early morning specimen for smear and culture and drug susceptibility testing.
- Providing VCT and encouraging health care personnel to know their HIV status
- Advocating / providing precautionary measures for HIV positive staff, such as TB preventive therapy (IPT) and antiretroviral therapy.
- Appropriate placement of HIV positive staff in low TB risk areas of the facility.

17.2 Medical surveillance programme

Pre – placement screening

Staff protection begins with pre-employment screening. This aims to assess risk and detect disease early to ensure appropriate interventions. It includes:

- Recording any history or symptoms of tuberculosis
- Family history of TB
- Risk factors for TB
- Documentary evidence of baseline test results - Mantoux skin test, chest x-rays, HIV, Blood glucose

All staff with TB symptoms should have a medical assessment and investigations to exclude active TB.

All staff should be educated about TB symptoms, prevention and treatment. Information on where and when to seek medical care must be provided.

Periodic medical examinations
This screening will identify staff who have TB disease or new TB infection, without a known M. TB exposure, and are therefore, at increased risk of progression to TB disease.

Periodic examinations should be conducted six monthly and should include;
- Medical history
- TB symptom review
- TST
- Physical assessment
- Chest x-ray
- Other tests, as appropriate

Exit medical examination
This is conducted when staff are transferred from a high risk area, leave employment (retirement or for other reasons).

Medical leave
All HCWs confirmed to have active pulmonary TB infection should be given medical leave at least two weeks or until the AFB negative on smear microscopy.

Return to work policy
HCW with TB should be allowed to return to work when they have received adequate treatment, the cough has resolved, have been confirmed to be non infectious (smear microscopy negative for AFB) and are physically fit to perform their normal duties.

On resumption of duty the HCW must be provided with treatment and psycho social support for the duration of treatment. Monthly follow up for clinical and bacteriological monitoring by treating physician must be adhered to.

Medical records
Medical information obtained from the staff during the examinations must be kept confidential. Access to the medical records should be limited to occupational health or designated staff only. The following information must be documented;
- Name, designation, date of employment/ assignment to facility
- Results of baseline assessment
- TB symptom screening questionnaires
- Clinical examination findings
- Mantoux test results
- Chest x-ray
- Referral for medical evaluation
- Bacteriology results for those investigated for TB
- Treatment received
- Completion of treatment for TB infection or TB disease

18. MONITORING AND EVALUATION

A key element of the DOTS Strategy is the establishment and maintenance of a system to monitor case detection and treatment outcomes. A monitoring and evaluation (M&E) system is essential to programme management since it provides the basis for assessing progress made towards achieving programme goals. In addition, it allows the size of the tuberculosis problem and its evolution over time to be evaluated.

Staff and managers need to have a thorough understanding of the content and process of TB programme monitoring and evaluation to enable them plan adequately and to use information to drive service improvements. M&E is an important management tool at every level in programme management. It plays an important role in the day-to-day management of health programmes and provides programme managers with the information and insight needed for strategic planning, programme design and implementation, and decision-making about human and financial resources, especially in resource-limited settings.

M&E provides an indication of how well objectives have been achieved, whether activities have been undertaken as intended and whether services are effective in reaching programme goals. It can be used to address weaknesses in programme design and implementation. Using information in decision-making can help to ensure accountability of staff and managers. A good M&E system is required at every level in the health system, characterized by the following:

- Clear goals, objectives and targets (that are cumulative, with facility targets leading to sub-district targets leading to district targets leading to provincial targets leading to national targets)
- The selection of indicators which are valid, reliable, specific, operationally feasible and comparable over time and in different districts, provinces and countries
- Quality assurance procedures to ensure that quality data is collected
- The timely submissions and processing of data
- The ability to process and analyse data
- Data dissemination in both directions
- Both monitoring and evaluation are done on a “cohort” basis. This ensures that all patients recorded in the register within a specified calendar quarter are accounted for within the analysis.

18.1 Monitoring

Monitoring is the routine tracking of key elements of programmes performance through careful record keeping and regular reporting. Monitoring is used to assess whether or not activities are carried out as planned. It focuses on the activities implemented and results achieved. It provides continuous information on the progress being made to achieve goals and alerts staff and managers to problems, providing an opportunity for these to be resolved early.

Effective monitoring relies on accurate records being maintained for all patients and periodic, regular reporting of activities. The tools that have been developed by the TB Programme help standardise the way in which information is collected.

18.2 Evaluation

Evaluation is an episodic, in-depth analysis of programme performance. It assesses progress towards operational targets and epidemiological objectives. It relies on data generated through routine information as well as from other sources such as research studies. There are various types of evaluation;

- Process evaluation measures the quality of programme implementation and assesses coverage.
- Outcome and impact evaluations measure programme results and the effect on the target population.
- Outcome evaluations also measure the extent to which stated objectives are achieved with respect to the programme's goals.

Evaluation is an essential management tool, not only for the analysis of results, but also for the management of the TB programme, particularly for guiding implementation, ordering drugs and laboratory reagents, training of health staff, identifying problems in service delivery and eventually the expansion of the health structures involved in the TB programme. Regular evaluation is required not simply for surveillance purposes but is necessary for efficient management of the programme. An evaluation of the extent to which targets set by the TB programme are reached helps identify parts of the programme that are not functioning well. Regular collation of essential information is an integral part of the routine operations of the TB programme and should not be compromised or minimized due to other pressures.

18.3 Surveillance

Surveillance is the routine collection of epidemiological data (i.e. disease outcomes) to track trends in disease incidence or prevalence over time. Data may be collected through seroprevalence surveys or through the routine reporting of cases seen by health facilities. Although surveillance data is an important source for M&E, surveillance should not be confused with, or substituted for, actual programme monitoring.

18.4 Standard tools used in the TB Programme

The following tools used by the TB programme:

1) TB Identification and Follow Up Register (GW 20/13): Used at facility level to record symptomatic patients reporting to that facility, to assist the follow-up of results and initiation of treatment.
2) Laboratory request form for Sputum Examination: A specific TB laboratory request form, available from the National Health Laboratory should be used by all facilities. Correct completion can help assess case-finding.
3) TB Treatment Record (GW 20/12): The blue clinic/hospital card is used in all facilities to collect all the information about the patient, treatment and outcomes (demographic, disease classification, treatment regimen, monitoring and outcomes). This is the source document used to complete the register.
4) TB Patient treatment card (GW 20/15): The green patient-held card is used to record details of treatment including daily doses taken for all TB patients on treatment.
5) Tuberculosis Register (GW 20/11): Used in all facilities to summarise key information from the clinic / hospital card on each registered patient (demographic, disease classification, treatment regimen, monitoring and outcomes). Information from the register is collated electronically and forms the basis for monitoring and evaluation of the TB programme. The register needs to be updated on a daily basis. It provides an overview of all registered patients and should be used as a clinical and programme management tool at facility level.
6) Transfer form (GW20/14): Used in all facilities to report on the key patient information from the register when the patient is transferred/moved from one district/facility to another.
7) TB symptom screening tool
8) Notification of Notifiable Medical Conditions Form
9) TB Daily Diary

18.5 Cascade analysis at facility level

Facilities must conduct a cascade analysis of the data from suspicion to treatment outcome on a monthly and quarterly basis. This will help to identify leakages or gaps in patient management within the facility and enable the facility to implement strategies to address them early preventing adverse treatment outcomes. The data elements for cascade analysis are presented in the table below.

DATA ELEMENTS	DESCRIPTION
TB DETECTION	
Total PHC Headcount	Total number of patients seen at the facility (OPD in case of hospital)
Number of patients screened for TB symptoms	This includes all patients screened using the symptom screening tool. *Source document:* TB symptom screening Book
Number of patients found to have TB symptoms	Includes all patients with a positive symptom screen (with or without a cough) *Source document:* TB symptom screening Book
Number of patients with TB symptoms tested for TB	Includes all tests conducted (bacteriology, histology, chemistry, x-rays) to confirm TB in the patient. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document:* TB identification register
Number of patients tested for TB with a positive TB result	Includes all tests conducted (bacteriology, histology, chemistry, x-rays) to confirm TB in the patient. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document:* TB identification register
Number of patients tested positive for TB started on TB treatment	All TB patients who are started on treatment. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document:* TB register
CONTINUUM OF CARE (Cohort analysis)	
Number of TB patients successfully completing the intensive phase of treatment	Total number of ALL TB patients who completed intensive phase of treatment at 2 months and changed to continuation phase
Number of TB patients successfully completing treatment	Total number of patients who are cured and those who completed treatment at the end of the continuation phase (6 -9 months)

18.6 The electronic TB register

The electronic TB register (ETR.net) is a programme management tool used at sub/district level. The information submitted to the sub/district is entered into the electronic register and data validation and analysis is done using this tool.

The following reports can be generated by the system for a specified period or as a summary over time:

- Reports on TB patients registered
- Reports on Sputum Conversion
- Reports on Treatment Outcome
- Facility Profile Reports

Data is transmitted electronically from the sub/district level to the provincial level where it is aggregated and analysed before it is passed on to the national level. Specific data elements are exported to the district health information system (DHIS) at sub/district level.

18.7 Standard reports

The following reports should be analysed on a quarterly basis:

1) **Quarterly report on All TB patients registered/ notified:** Completed at sub/district level and reports on the completed quarters cohort.
2) **Quarterly report on smear conversion:** Completed at sub/district level and reports on the previous quarter's cohort.
3) **Quarterly report on treatment outcomes for new and retreatment smear positive pulmonary TB and All TB patients:** Completed at sub/district for the cohort registered 9 months earlier.
4) **Quarterly report on HIV indicators:** Completed at sub/district for the cohort registered 9 months earlier.
5) **Quarterly report on programme management:** Compiled at sub/district level, and is mainly a narrative report.

18.8 Information flow

Information is collected at facility level in the patient-held green card and blue clinic or hospital record card and used to update the register. This should be done on a regular (daily) basis. Good data is dependent on the quality of information in the paper-based TB registers. These need to be reviewed throughout the month for completeness and correctness. As soon as a TB register sheet is completed, it needs to be sent to the sub-district office for data capturing. TB Register sheets (pink, yellow and green) must be sent to the sub-district office and data captured throughout the month to allow sufficient time for data validation and analysis at the end of a cohort period.

Timely reporting is central to effective programme management. Reporting on quarterly cohorts does not mean that data is collated on a quarterly; monthly data collation is required at the lowest level of care (facility, sub-district or district level). This will ensure that meaningful action is taken resulting in sub/ districts and provinces and ensure timeous reporting.

Recommended timelines for data collation:

- **In the 1st week after end of the month**, the TB Coordinator and sub-district data capturer / health information officer need to ensure that all the TB Register sheets due but still outstanding are collected.
- **In the 2nd week after end of the month**, the data capturer / health information officer needs to ensure that all outstanding data (new cases and updates) is captured.
- **During the 3rd week after end of the month**, the TB Coordinator and data capturer / health information need to run data checks and ensure that all the data that has been captured is correct and complete.
- **At the end of the 3rd week**, dispatch files need to be sent to the next level.

Due dates for final cohort reporting:

- Case finding data is due at the end of the quarter
- Smear conversion data is due 3 months after the end of the quarter
- Treatment outcome data is due 9 months after the end of the quarter.

In each instance, sub-district data should be submitted to the district within 3 weeks, district data submitted to the province a week later and provincial data submitted to the national office 1 week later. National data should be collated within a week and disseminated back to provinces.

Table 18.1: Information Processing and Flow

Patient records: Update on a daily and weekly basis
Facility TB Register (Paper-based): Update on a daily to weekly basis Submit TB Register sheets to the sub-district office weekly: *Pink sheets* – as soon as all patient identification information, disease information and pre-treatment sputum results have been entered. *Yellow sheets* – as soon as all the smear conversion sputum results at the end of the intensive phase (2 or 3 months) have been captured *Green sheets* – as soon as all outcomes have been recorded (the correct outcome as well as the outcome date).
Sub-district register (Electronic): Update on a weekly basis Run checks to validate data Submit reports to district level within 3 weeks of: End of quarter for case finding 3 months after end of quarter for smear conversion 9 months after end of quarter for treatment outcomes Generate facility reports (used to provide feedback to facilities)
District register (Electronic): Update on a quarterly basis Run checks to validate data Submit reports to provincial level within 4 weeks of: End of quarter for case finding 3 months after end of quarter for smear conversion 9 months after end of quarter for treatment outcomes Generate sub-district reports (used to provide feedback to sub-districts)
Provincial register (Electronic): Update on a quarterly basis Run checks to validate data Submit reports to national level within 5 weeks of: End of quarter for case finding 3 months after end of quarter for smear conversion 9 months after end of quarter for treatment outcomes Generate district reports (used to provide feedback to districts)
National register (Electronic): Update on a quarterly basis Run checks to validate data Collate National report within 6 weeks of: End of quarter for case finding 3 months after end of quarter for smear conversion 9 months after end of quarter for treatment outcomes Generate provincial reports (used to provide feedback to the provinces)

Timelines for Reporting			
Start of Treatment	Report	Level	Date of Analysis
01 January – 31 March	TB REGISTRATION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of April 1st Week of May 2nd Week of May
1 January – 31 March	SMEAR CONVERSION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of July 1st Week of August 2nd Week of August
	TREATMENT OUTCOME	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of January 1st Week of February 2nd Week of February
1 April – 30 June	TB REGISTRATION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of July 1st Week of August 2nd Week of August
	SMEAR CONVERSION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of October 1st Week of November 2nd Week of November
	TREATMENT OUTCOME	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of April 1st Week of May 2nd Week of May

1 July – 30 September	TB REGISTRATION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of April 1st Week of May 2nd Week of May
	SMEAR CONVERSION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of January 1st Week of February 2nd Week of February
	TREATMENT OUTCOME	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of July 1st Week of August 2nd Week of August
1 October – 31 December	TB REGISTRATION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of January 1st Week of February 2nd Week of February
	SMEAR CONVERSION	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of April 1st Week of May 2nd Week of May
	TREATMENT OUTCOME	Facility level Sub-district level District level Provincial level National	Monthly Monthly 4th Week of October 1st Week of November 2nd Week of November

Overall sub-district or district results can hide significant differences in programme performance between individual facilities. Data needs to be collated and analysed at facility level because this is the level at which quality improvements have to be made. It is recommended that on a quarterly basis standard

facility reports are generated and tracked over time.

An analysis of the facility data should answer the following questions:

- What does the data show?
- How is the facility performing in comparison to previous quarters?
- How well is the facility performing relative to the targets that have been set?
- In which areas is the facility performing well?
- Which are areas of concern?
- What can we learn from the things that we are doing well?
- What are the most important problems that should be addressed?
- What factors at different points in the TB service contribute to these problems?
- What activities will be undertaken to remedy the problems at each point in the service?
- What resources will be required to undertake the activities?
- Who will undertake each of the activities?
- What is the target set for each of the indicators where quality improvement is sought?
- How will the facility manager monitor whether these activities are undertaken?

Information from additional sporadic evaluation can be extremely useful in providing insights into the factors contributing to the facility's performance. This information may come from different sources such as the Facility Supervisory Checklist.

Trying to identify the underlying practices that contribute to poor programme performance is a challenge. All too frequently staff and managers become defensive and provide explanations for programme performance that are not borne out by the data available. Building data analysis skills and instilling the practice of self-reflection is necessary at all levels in the health system in working towards systematic improvements.

Programme monitoring indicators

TB Notification indicators

Indicator	Description	Source	Collection	Level
1. TB case notification rate	**Numerator:** Total TB patients reported in a year (× 100,000) **Denominator:** Total population in the same year	ETR.net	Quarterly	All
2. TB Detection rate	**Numerator:** Annual number of new TB patients notified **Denominator:** Annual estimated number of new TB patients	ETR.net Surveillance data	Annual	National
3. Bacteriological coverage	**Numerator:** Number of PTB patients diagnosed by bacteriological tests (Xpert, smear or culture) **Denominator:** Total PTB patients reported, excluding children 0–4 years	ETR.net	Quarterly	All
4. Proportion smear-positive pulmonary TB patients	**Numerator:** Number of smear positive pulmonary TB patients **Denominator:** Total number of pulmonary TB patients	ETR.net	Quarterly	All

Indicator	Description	Source	Collection	Level
5. Sputum results turnaround time*	**Numerator:** Number of smear positive results received from the laboratory within 48 hours of the specimen being taken (spot specimen) including weekends and public holidays. **Denominator:** Total number of smears submitted	TB Case Identification & Follow-up register	Quarterly	All
6. Xpert positivity rate	**Numerator:** Total number of positive Xpert results (MTB detected) **Denominator:** Total number of Xpert tests conducted over the same period	NHLS report	Quarterly	All

* Sub/districts report on the % of facilities that meet the target of 80% sputum TAT for all smear microscopy results within 48 hours

Case holding indicators

Indicator	Description	Source	Collection	Level
1. Time to treatment initiation rate	**Numerator:** Number of laboratory diagnosed TB patients started on treatment within 48 hours of diagnosis **Denominator:** Total number of laboratory diagnosed TB patients during the same period	TB identification & Follow-up register; TB register	Quarterly	All
2. New smear-positive conversion rates	**Numerator:** Number of new smear positive patients that convert from smear positive to smear negative at 2 months **Denominator:** Total number of new smear-positive patients	ETR.net	Quarterly	All
3. Retreatment smear-positive conversion rates	**Numerator:** Number of retreatment smear positive patients that convert from smear positive to smear negative at 2 months **Denominator:** Total number of retreatment smear-positive patients	ETR.net	Quarterly	All

TB and HIV indicators

Indicator	Description	Source	Collection	Level
1. HIV positivity rate	**Numerator:** Number of registered TB patients known to be HIV positive **Denominator:** Total number of registered TB patients	ETR.net	Quarterly	All
2. HIV positive TB patients on CPT	**Numerator:** Total number of registered HIV+ TB patients on CPT **Denominator:** Total number of registered TB patients known to be HIV positive	ETR.net	Quarterly	All
3. HIV+ TB patients on ART on completion of treatment	**Numerator:** Total number of registered HIV+ TB patients on ART at the end of treatment **Denominator:** Total number of registered HIV+ TB patients	ETR.net	Quarterly	All

These indicators are compiled at "Treatment outcome" rate.

TB treatment outcome indicators - new smear-positive pulmonary TB cases

Indicator	Description	Source	Collection	Level
1. Cure rates	**Numerator:** Number of new smear-positive patients that are smear negative in the last month of treatment and on at least one other occasion at least 30 days prior **Denominator:** Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
2. Treatment success rate	**Numerator:** Total number of new smear-positive patients that were cured and those that completed treatment but did not meet the criteria for cure or failure **Denominator:** Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
3. Loss to follow up rate	**Numerator**: Number of new smear-positive patients that interrupted treatment for 2 consecutive months or more **Denominator**: Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
4. Death rate	**Numerator**: Number of new smear-positive patients that died during treatment **Denominator**: Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
5. Treatment failure rate	**Numerator**: Number of new smear-positive patients that are smear-positive at the end of treatment period **Denominator**: Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
6. Transfer-out rate	**Numerator**: Number of new smear-positive pulmonary TB patients registered that were transferred to another district and for whom the treatment outcome is unknown **Denominator**: Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All
7. Not evaluated rate	**Numerator**: Number of new smear-positive patients that have no outcome at the end at the end of the treatment **Denominator**: Total number of new smear-positive pulmonary TB patients registered	ETR.net	Quarterly	All

TB Treatment outcome indicators - retreatment smear-positive pulmonary TB patients

Indicator	Description	Source	Collection	Level
1. Cure rates	**Numerator:** Number of retreatment smear-positive patients that are smear negative in the last month of treatment and on at least one other occasion at least 30 days prior **Denominator:** Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All
2. Treatment success rate	**Numerator:** Total number of retreatment patients that were cured and those that completed treatment but did not meet the criteria for cure or failure **Denominator:** Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All
3. Loss to follow up rate	**Numerator:** Number of retreatment smear-positive patients that interrupted treatment for 2 consecutive months or more **Denominator:** Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All
4. Death rate	**Numerator:** Number of retreatment smear-positive patients that died during treatment, irrespective of cause **Denominator:** Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All
5. Failure rate	**Numerator:** Number of retreatment smear-positive patients that are smear-positive at the end of treatment **Denominator:** Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All
6. Transfer-out rate	Numerator: Number of retreatment smear-positive pulmonary TB patients registered that were transferred to another district and for whom the treatment outcome is unknown Denominator: Total number of retreatment smear -positive pulmonary TB patients registered during the same period	ETR.net	Quarterly	All
7. Not evaluated rate	Numerator: Number of retreatment smear-positive patients that have no outcome at the end of treatment Denominator: Total number of retreatment smear -positive pulmonary TB patients registered	ETR.net	Quarterly	All

TB Treatment outcome indicators - All TB patients

Indicator	Description	Source	Collection	Level
1. Treatment Success rate	**Numerator:** Sum of number patients that were cured and those who completed treatment but did not meet the criteria for cure or failure **Denominator:** Total number of All TB patients registered	ETR.net	Quarterly	All
2. Loss to follow up rate	**Numerator:** Number of All registered TB patients that interrupted treatment for more than 2 consecutive months **Denominator:** Total number of All TB patients registered	ETR.net	Quarterly	All
3. Death rate	**Numerator:** Number of All registered TB patients that died during treatment, irrespective of cause **Denominator:** Total number of All TB patients registered	ETR.net	Quarterly	All
4. Failure rate	**Numerator:** Number of All registered TB patients that are smear/ culture-positive 5 months or later after initiating treatment or that are diagnosed as MDR-TB during treatment **Denominator:** Total number of All TB patients registered	ETR.net	Quarterly	All
5. Transfer-out rate	**Numerator:** Number of All registered TB patients registered that were transferred to district/ province/ country and for whom there is no treatment outcome information **Denominator:** Total number of All TB patients registered during the same period	ETR.net	Quarterly	All
6. Not evaluated rate	**Numerator:** Number of All TB patients that have no outcome at the end of the treatment and that did not complete the full course of treatment **Denominator:** Total number of All TB patients registered	ETR.net	Quarterly	All

Laboratory indicators (Xpert)

Indicator	Description	Collection	Level
Number of Xpert tests conducted	Total number of Xpert tests conducted during the reporting period	Monthly	All
Number MTB detected	Number of test results that were positive	Monthly	All
Number MTB not detected	Number of test results that were negative	Monthly	
Number of tests unsuccessful	Number of tests that did not have a result (due to failure of cartridge of machine)	Monthly	All
Number Rif susceptible	Number of positive test results that were Rifampicin susceptible	Monthly	All
Number Rif resistant	Number of positive test results that were Rifampicin resistant	Monthly	All
Number Rif result inconclusive	Number of positive test results that did not have a clear result confirming Rifampicin susceptibility or resistance	Monthly	All
Number no Rif result	Number of positive test results that did not have a Rifampicin DST result	Monthly	All
Sputum specimen rejection rate	**Numerator:** Number of sputum specimen rejected for testing by the labratory **Denominator:** Total number of specimen received for testing by the laboratory during the same period	Monthly	

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ANNEXURE 1:
TUBERCULIN SKIN TESTING

The tuberculin skin test (TST) has limited value in clinical work, especially where TB is common. The test shows hypersensitivity to proteins of the TB bacillus, as a result either of infection with M. tuberculosis or induced by Bacille Calmette-Guérin (BCG) vaccination. It indicates infection and not TB disease. In children, infection is one of the criteria used in the diagnosis of TB. In adults, it is used to diagnose latent infection in immunosuppressed patients who would benefit from INH prophylactic therapy.

The test involves injecting tuberculin purified protein derivative (PPD) into the skin. Previous exposure results in a local delayed type hypersensitivity reaction within 24-72 hours. The reaction is identified as palpable induration (hardness) at the site of injection. The response only indicates hypersensitivity. It shows that the person has at some time been infected with M. tuberculosis or been vaccinated. By itself, it does not indicate the presence or extent of tuberculosis disease.

The reaction after previous BCG is usually weaker than the reaction to natural infection and remains positive for several years thereafter. It should also be noted that a negative result does not rule out the diagnosis of TB disease. Various conditions, including HV may suppress the reaction.

Performing a Mantoux Tuberculin Skin Test

1) The Mantoux TST is the most reliable test available. The test requires:
   - 2 units of tuberculin purified protein derivative PPD-RT23 2TU or
   - 5 units of PPD-S 5TU.
2) Use a single-dose tuberculin syringe and a short 27-gauge needle with a short bevel to do the test.
3) Draw up 0.1ml of PPD of the correct strength into the syringe.
4) Clean an area of skin in the mid anterior section of the forearm. The PPD is injected between layers of skin (intradermally). 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) 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.
6) 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.

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

Interpreting a positive TST

- A positive test indicates infection with TB, but not necessarily TB disease.
- In a child under 5 years or an 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 other features such as 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
- Children under the age of 5 years, HIV-infected children of any age and HIV-infected adults, who have a positive skin test and no symptoms or signs of TB, should be put on TB prophylaxis for six months.

Interpreting a negative TST

A negative tuberculin skin test does not exclude TB; various conditions may cause a false negative reaction including:

- HIV infection
- Malnutrition
- Severe viral infections (e.g. measles, chicken pox)
- Cancer
- Immuno-suppressive drugs (e.g. steroids)
- Severe disseminated TB.

ANNEXURE 2:
ESSENTIAL TUBERCULOSIS MEDICINES

1. Isoniazid

Group:	*antimycobacterial agent*
Tablet:	100mg, 300mg
Injection:	25 mg/ ml (in 2-ml ampoule)

General information

Isoniazid, the hydrazide of isonicotinic acid is highly bactericidal against replicating tubercle bacilli. It is rapidly absorbed and diffuses readily into all fluids and tissues. The plasma half-life, which is genetically determined, varies from less than one hour in fast acetylators to more than three hours in slow acetylators. It is largely excreted in the urine within 24 hours, mostly as inactive metabolites.

Clinical information

1) Uses

A component of all TB chemotherapeutic regimens currently recommended by WHO

Isoniazid alone is occasionally used to prevent:

- Transmission to close contacts at high risk of disease.
- Progression of infection to primary complex in recently infected, asymptomatic individuals.
- Development of active TB in immunodeficient individuals.

2) Dosage and administration

Isoniazid is normally taken orally but it may be administered intramuscularly to critically ill patients.

3) Treatment (combination therapy)

Adults 5 (4-6) mg/kg daily, maximum 300 mg
Children 10 (8-12) mg/kg daily, maximum 300 mg

4) Preventive therapy:

Adults: 300 mg daily for six months at least
Children: 10 mg/kg daily (maximum 300 mg) for six months at least

Contraindications:

- Known hypersensitivity
- Active hepatic disease

Precautions

- Monitoring of serum concentrations of hepatic transaminases, where possible, is useful in patients with pre-existing chronic liver disease.
- Patients at risk of peripheral neuropathy as a result of malnutrition, chronic alcohol dependence or diabetes should additionally receive pyridoxine, 10-50 mg daily. Where the standard of health in the community is low, this should be offered routinely.
- Isoniazid interacts with anti-convulsants used for epilepsy. It may be necessary to reduce the dosage of these drugs during treatment with isoniazid.

Use in pregnancy
Whenever possible, the six-month regimen based upon isoniazid, rifampicin and pyrazinamide should be used.

Adverse effects
- Isoniazid is generally well tolerated at recommended doses. Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment.
- The risk of peripheral neuropathy is excluded if vulnerable patients receive daily supplements of pyridoxine. Other less common forms of neurological disturbance, including optic neuritis, toxic psychosis arid generalized convulsions, can develop in susceptible individuals, particularly in the later stages of treatment and occasionally necessitate the withdrawal of isoniazid.
- Hepatitis is an uncommon but potentially serious reaction that can usually be averted by prompt withdrawal of treatment. More often, however, a sharp rise in serum concentrations of hepatic transaminases at the outset of treatment is not of clinical significance, and usually resolves spontaneously during continuation of treatment.

Drug interactions
- Isoniazid tends to raise plasma concentrations of phenytoin and carbamazepine by inhibiting their metabolism in the liver.
- The absorption of isoniazid is impaired by aluminium hydroxide.

Overdosage
- Nausea, vomiting, dizziness, blurred vision and slurring of speech occur within 30 minutes to three hours of overdosage.
- Massive poisoning results in coma preceded by respiratory depression and stupor. Severe intractable seizures may occur. Emesis and gastric lavage, activated charcoal, anti-epileptics and IV sodium bicarbonate can be of value if instituted within a few hours of ingestion. Subsequently, haemodialysis may be of value. Administration of high doses of pyridoxine is necessary to prevent seizures.

Storage
Tablets should be kept in well-closed containers, protected from light. Solution of injection should be stored in ampoules protected from light

2 Rifampicin

Group: *antimycobacterial agent*
Capsule or tablet: 150 mg, 300 mg

General information
A semi synthetic derivative of rifamycin, a complex macrocyclic antibiotic, inhibits ribonucleic acid synthesis in a broad range of microbial pathogens. It has bactericidal action and a potent sterilizing effect against tubercle bacilli in both cellular and extra cellular locations. Rifampicin is lipid-soluble. Following oral administration, it is rapidly absorbed and distributed throughout the cellular tissues and body fluids; if the meninges are inflamed, significant amounts enter the cerebrospinal fluid.

A single dose of 600 mg produces a peak serum concentration of about 10 micrograms/ml in two to four hours, which subsequently decays with a half-life of two to three hours. It is extensively recycled in the enterohepatic circulation, and metabolites formed by deacetylation in the liver are eventually excreted in the faeces. Since resistance readily develops, rifampicin must always be administered in combination with other effective antimycobacterial agents.

Clinical information
Uses
A component of all six and eight month TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration
Rifampicin should preferably be given at least 30 minutes before meals, since absorption is reduced when it is taken with food. This however may not be clinically significant and food can reduce intolerance to drugs.

Adults and children: 10 mg/kg (8-12 mg/kg) daily, maximum 600mg daily, two or three times weekly.

Contra-indications
- Known hypersensitivity to rifamycins
- Hepatic dysfunction

Precautions
- Serious immunological reactions resulting in renal impairment, haemolysis or thrombocytopenia are on record in patients who resume taking rifampicin after a prolonged lapse of treatment. In this rare situation it should be immediately and definitely withdrawn.
- Careful monitoring of liver function is required in the elderly and in patients who are alcohol-dependent or have hepatic disease. Patients should be warned that treatment may produce reddish coloration of urine, tears, saliva and sputum, and that contact lenses may be irreversibly stained.

Use in pregnancy
Whenever possible, the six-month regimen based upon isoniazid, rifampicin and pyrazinamide should be used.

Vitamin K should be administered at birth to the infant of a mother taking rifampicin because there is a risk of postnatal haemorrhage.

Adverse effects
- Rifampicin is well tolerated by most patients at currently recommended doses, although gastrointestinal intolerance can be unacceptably severe.
- Other adverse effects (fever, influenza-like syndrome and tbrombocytopenia) are more likely to occur with intermittent administration, and skin rashes just as likely.
- Exfoliative dermatitis is more frequent in HIV positive TB patients.
- Temporary oliguria, dyspnoea and haemolytic anaemia have also been reported in patients taking the drug three times weekly. These reactions usually subside if the regimen is changed to one with daily dosage.
- Moderate rises in serum concentrations of bilirubin and transaminases, which are common at the outset of treatment, are often transient and without clinical significance. However, dose-related hepatitis can occur which is potentially fatal. It is consequently important not to exceed the maximum recommended daily dose of 10 mg/kg (600 mg).

Drug interactions
- Rifampicin induces hepatic enzymes, and may increase the dosage requirements of drugs metabolized in the liver. These include corticosteroids, steroid contraceptives, oral hypoglycaemic agents, oral anticoagulants, phenytoin, cimetidine, cyclosporin and digitalis glycosides.
- Since rifampicin reduces the effectiveness of the oral contraceptive pill, women should consequently be advised to choose between one of the following two options for contraception.
- Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of oestrogen (50mcg).
- Alternatively she could use a non-hormonal method of contraception throughout rifampicin treatment and for at least one month subsequently. Current antiretroviral drugs (non-nucleoside reverse transcriptase inhibitors and protease inhibitors) interact with rifampicin. This may result in the ineffectiveness of antiretroviral drugs, ineffective treatment of TB or an increased risk of drug toxicity. Biliary excretion of radiocontrast media and sulfobromophthalein sodium may be reduced and microbiological assays for folic acid and vitamin B12 disturbed.

Overdosage
Gastric lavage may be of value if undertaken within a few hours of ingestion. Very large doses may depress central nervous function. There is no specific antidote and treatment is supportive.

Storage
Capsules and tablets should be kept in tightly closed containers, protected from light.

3 Pyrazinamide

Group: *antimycobacterial agent*
Tablet: 400 mg

General information
A synthetic analogue of nicotinamide that is only weakly bactericidal against M tuberculosis, but has potent sterilizing activity, particularly in the relatively acidic intracellular environment of macrophages and in areas of acute inflammation. It is highly effective during the first two months of treatment while acute inflammatory changes persist and its use has enabled treatment regimens to be shortened and the risk of relapse to be reduced. It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout all tissues and fluids. Peak plasma concentrations are attained in two hours and the plasma half-life is about 10 hours. It is metabolized mainly in the liver and is excreted largely in the urine.

Clinical information
Uses
A component of all six and eight month TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration
Adults and children (for the first two or three months):
25 mg/kg (20-30 mg/kg) daily
35 mg/kg (30-40 mg/kg) three times weekly

Contraindication
- Known hypersensitivity
- Severe hepatic impairment

Precautions
- Patients with diabetes should be carefully monitored since blood glucose concentrations may become labile.
- Gout may be exacerbated.

Use in pregnancy
The six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used whenever possible.

Adverse effects
- Pyrazinamide may cause gastro intestinal intolerance.
- Hypersensitivity reactions are rare, but some patients complain of slight flushing of the skin.
- Moderate rises in serum transaminase concentrations are common during the early phases of treatment. Severe hepatotoxicity is rare.
- As a result of inhibition of renal tubular secretion, a degree of hyperuricaemia usually occurs, but this is often asymptomatic. Gout requiring treatment with allopurinol occasionally develops. Arthralgia, particularly of the shoulders, may occur and is responsive to simple analgesics (aspirin). Both hyperuricaemia and arthralgia may be reduced by prescribing regimens with intermittent administration of pyrazinamide.

Overdosage
Little has been recorded of pyrazinamide overdose. Acute liver damage and hyperuricaemia have been reported. Treatment is essentially symptomatic. Emetic and gastric lavage may be of value if undertaken within a few hours of ingestion. There is no specific antidote and treatment is supportive.

Storage
Tablets should be stored in tightly closed containers, protected from light.

4 Streptomycin

General information
An aminoglycoside antibiotic derived from Streptomyces griseus that is used in the treatment of TB and sensitive Gram-negative infections. Streptomycin is not absorbed from the gastrointestinal tract but, after intramuscular administration, it diffuses readily into the extracellular component of most body tissues and it attains bactericidal concentrations, particularly in tuberculous cavities. Little normally enters the cerebrospinal fluid, although penetration increases when the meninges are inflamed. The plasma half-life, which is normally two to three hours, is considerably extended in the new-born, in the elderly and in patients with severe renal impairment. It is excreted unchanged in the urine.

Clinical information
Uses A component of several TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration
Streptomycin must be administered by deep intramuscular injection.
Adults and children
15 mg/kg (12-18 mg/kg) daily
Patients over 60 years may not be able to tolerate more than 500-750 mg daily.

Contraindications
- Known hypersensitivity
- Auditory nerve impairment
- Myasthenia gravis

Precautions
- Hypersensitivity reactions are rare; if they occur (usually during the first weeks of treatment) streptomycin should be withdrawn immediately. Once fever and skin rash have resolved, desensitization may be attempted.
- Streptomycin should be avoided, when possible, in children because the injections are painful and irreversible auditory nerve damage may occur.
- Both the elderly and patients with renal impairment are also vulnerable to dose-related toxic effects resulting from accumulation. Where facilities are available to monitor and function closely it may be possible to give streptomycin in reduced doses to patients with renal impairment. Where possible, serum levels should be monitored periodically and dosage adjusted appropriately to ensure that plasma concentrations, as measured when the next dose is due, do not rise above 4 mg/mI.
- Protective gloves should be worn when streptomycin injections are administered, to avoid sensitisation dermatitis.

Use in pregnancy
Streptomycin should not be used in pregnancy. It crosses the placenta and can cause auditory nerve impairment and nephrotoxicity in the fetus.

Adverse effects

- Injections are painful and sterile abscesses can form at injection sites.
- Hypersensitivity reactions are common and can be severe. Impairment of vestibular function is uncommon with currently recommended doses.
- Dosage should be reduced if headache, vomiting, vertigo and tinnitus occur.
- Streptomycin is less nephrotoxic than other aminoglycoside antibiotics. Dosage must be reduced by half immediately if urinary output falls, if albuminuria occurs or if tubular casts are detected in the urine.
- Haemolytic anaemia, aplastic anaemia, agranulocytosis, thrombocytopenia and lupoid reactions are rare adverse effects.

Drug interactions

- Other ototoxic or nephrotoxic drugs should not be administered to patients receiving streptomycin. These include other aminoglycoside antibiotics, amphotericin B, cefalosporins, etacrynic acid, cyclosporin, cisplatin, furosemide and vancomycin.
- Streptomycin may potentiate the effect of neuromuscular blocking agents administered during anaesthesia.

Overdosage

Haemodialysis can be beneficial. There is no specific antidote and treatment is supportive.

Storage

Solutions retain their potency for 48 hours after reconstitution at room temperature and for up to 14 days when refrigerated. Powder for injection should be stored in tightly closed containers protected from light.

5 Ethambutol

Group: *antimycobacterial agent*
Tablet: 100 mg, 400 mg (hydrochloride)

General information

A synthetic congener of I ,2-ethanediamine that is active against M. tuberculosis, M. bovis and some non-specific mycobacteria. It is used in combination with other TB drugs to prevent or delay the emergence of resistant strains. It is readily absorbed from the gastrointestinal tract. Plasma concentrations peak in 2-4 hours and decay with a half-life of 3-4 hours. Ethambutol is excreted in the urine both unchanged and as inactive hepatic metabolites, about 20% is excreted in the faeces as unchanged drug.

Clinical information

Uses

An optional component of several TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration

Adults: 15 mg/kg (15-20 mg/kg) daily
Children: maximum 15 mg/kg daily

Dosage must always be carefully calculated on a weight basis to avoid toxicity, and should be reduced in patients with impaired renal function.

Contraindications

- Known hypersensitivity.
- Pre-existing optic neuritis from any cause.
- Creatinine clearance of less than 50 ml/minute.

Precautions
Patients should be advised to discontinue treatment immediately and to report to a doctor should their sight or perception of colour deteriorate. Whenever possible, renal function should assessed before treatment.

Use in pregnancy
The six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used.

Ethambutol should be used if a fourth drug is needed during the initial phase.

Adverse effects
- Dose-dependent optic neuritis can result in impairment of visual acuity and colour vision. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly. Ocular toxicity is rare when used for 2-3 months at recommended doses.
- Signs of peripheral neuritis occasionally develop in the legs

Overdosage
Emesis and gastric lavage may be of value if undertaken within a few hours of ingestion. There is no specific antidote and treatment is supportive.

Storage
Tablets should be stored in well-closed containers.

ANNEXURE 3:
SIDE-EFFECTS OF INDIVIDUAL TB MEDICINES AND THEIR MANAGEMENT

1 ISONIAZID (H)

Adverse effects:

- Peripheral neuropathy (tingling and numbness of the hands and feet)
- Hepatitis, more often in patients older than 35 years (rare)
- Generalised skin rash (rare)
- Fever
- Joint pains

Management:

- **Mild itching:** Continue drug treatment; reassure the patient; give calamine lotion and if necessary antihistamine.
- **Fever and generalised skin rash:** Stop all drugs and give antihistamine.
- **Neuropathy:** Give 10 mg -25 mg of pyridoxine, daily.
- **Drug induced hepatitis:** Stop TB treatment; do liver function tests. If there is a loss of appetite, jaundice and liver enlargement, do not give treatment for at least 1 week or until the liver functions have returned to normal. In most patients INH can usually be given later without the return of hepatitis.

Drug interactions:

- Isoniazid inhibits the breakdown of epileptic drugs such as phenytoin and carbamazepine. Dosages of these drugs may need to be reduced during the treatment period.

2 RIFAMPICIN (R)

Adverse effects:

- **Gastro-intestinal:** nausea, anorexia and mild abdominal pain; diarrhoea occurs less frequently.
- **Cutaneous reactions:** mild flushing and itchiness of the skin.
- **Hepatitis:** This is uncommon unless the patient has a history of liver disease or alcoholism.
- Serious side effects like influenza syndrome and shock may occur in patients who take the medicine intermittently instead of daily. Stop the treatment and refer the patient.
- The patient should be warned that rifampicin colours the urine, sweat and tears pink (urine looks orange-pink).

Drug interactions:

- Rifampicin stimulates liver enzymes, which may break down other drugs more rapidly than normal e.g. oral anticoagulants (warfarin), oral diabetic drugs, digoxin, phenobarbitone and other anti-epileptics.
- **Contraception:** The dose of contraceptives should be increased in patients on rifampicin. Depo provera 150mg should be given 8 weekly instead of 12 weekly. Nur-Isterate 200mg should be given 6 weekly instead of 8 weekly. Combined oral contraceptives with at least 0.05mg of ethinyloestradiol should be prescribed. The pill free interval should be shortened from 7 to 4 days. Intra Uterine Contraceptive Devices (IUCDs) may be recommended. Warn the patient that the effect of rifampicin may last up to 2 months after the treatment is stopped.

3 STREPTOMYCIN (S)

Adverse effects:

- Cutaneous hypersensitivity, rash and fever.
- Ototoxicity (damage to eighth cranial nerve). Damage to the vestibular (balancing) apparatus causes dizziness, sometimes with vomiting. Unsteadiness is more marked in the dark. Can cause deafness.
- Deafness in unborn children. Streptomycin should be avoided during pregnancy because it crosses the placenta.
- **Anaphylaxis:** Streptomycin injection may be followed by tingling around the mouth, nausea and occasionally by sudden collapse. Treat as for any anaphylactic reaction and do not give streptomycin again.

Management:

- **Skin reactions:** treat as for allergic skin reactions.
- **Damage to vestibular apparatus:** treatment must be stopped immediately.
- **Ringing in the ears or loss of hearing:** if the drug is stopped immediately, the symptoms will usually clear over weeks. If not, the damage will be permanent.

Contra-indications:

- Do not give streptomycin to pregnant women (it crosses the placenta and can cause ototoxicity and nephrotoxicity in the foetus).
- Should be avoided where possible in children because injections are painful and it can cause irreversible auditory nerve damage.
- Do not give to patients with existing renal disease, as it will further impair renal function.
- Do not give to patients with myasthenia gravis.
- Older people (>65 years) have reduced renal function and the dosage may need to be reduced.

4 ETHAMBUTOL (E)

Adverse effects:

- Progressive loss of vision caused by retrobulbar neuritis, usually manifests first as loss of colour vision and usually presents after the patient has been on treatment for at least two months. This is usually caused by excessive doses of ethambutol.
- Skin rash.
- Joint pains.
- Peripheral neuropathy.

Management:

- If the patient complains about visual disturbance, stop treatment immediately.
- Skin rashes and joint pains usually respond to symptomatic treatment.

Contra-indication:

- Ethambutol should not be given if there is pre-existing optic neuritis or creatinine clearance is less than 50ml/min

5 PYRAZINAMIDE (Z)

Adverse effects:

- **Liver damage:** Anorexia, mild fever, tender enlargement of the liver and spleen may be followed by jaundice.

- **Arthralgia:** This is common and mild. The pain affects both large and small joints, the level of uric acid is increased and gout may occur.
- Skin rash on sun exposed areas.

Management:

- **Hepatotoxicity:** Do not give the drug again if severe hepatitis occurs.
- **Arthralgia:** Treatment with aspirin is usually sufficient. Allopurinol may be required for the treatment of gout.

Contra-indication:

- Should not be given with severe hepatic impairment.

6 PYRIDOXINE

- It is unnecessary to give pyridoxine routinely.
- The use of alcohol during drug therapy should be discouraged or restricted.
- However, pyridoxine should be added for TB patients who are alcohol abusers, pregnant, diabetic or epileptic. The protective dose is 10-25 mg daily. This dose should never be exceeded in pregnancy.

ANNEXURE 4:
COMPOSITION OF AN OUTBREAK RESPONSE TEAM AND ROLES

Provincial TB Program Manager

- Makes decision together with the district management team to develop and implement the response plan
- Provides leadership and overall management of activities of the team
- Provides, along with local coordinator, recommendations related to TB response, including legal issues
- Provides clinical and public health guidance to the team on issues such as contact investigations, isolation, infection control and treatment.
- Reviews all reports, publications, and other documents related to the response prior to use or distribution
- Convenes the team for evaluation of outbreak response
- Coordinates inter-district/ provincial communication (in cross border areas), including provider/ public alerts and advisories

District TB Coordinator

- Reviews the available district data to determine an outbreak
- Makes decision along with the district management team to request assistance from the province
- Provides final decisions related to outbreak response
- Provides clinical and public health guidance
- Reviews all reports, publications, and other documents related to TB response prior to use or distribution
- Maintains communication with relevant stakeholders in district
- Coordinates intra-district communication, including provider/ public alerts and advisories
- May serve as primary media spokesperson

National Health Laboratory Services Representative

- Provides sputum bottles, forms and bags specimen collection as needed
- Ensures smear microscopy services are ready for the increased demand for tests
- Facilitates the transportation of specimens to relevant tertiary laboratories where rapid assays for DR-TB and genotyping can be conducted.
- Reports test results to the district coordinator and primary health care provider within 24 hours of diagnosis being confirmed
- Maintains communication with the district coordinator and provincial TB programme manager

Epidemiologist

- Provides guidance for management of data on TB patients and contacts (i.e. epidemiologic analysis) and evaluation of outbreak response
- Ensures quality of ongoing TB surveillance and genotyping data
- Prepares communications and written reports related to outbreak response
- Maintains communication with district coordinator and provincial TB programme manager

Health Facility Nurse

- Investigate and report suspected and confirmed TB patients to district
- Provide TB case management and support; document all laboratory results (i.e. smear, culture, susceptibility, rapid assay, HIV status, genotyping)
- Conduct contact investigation specifically through identification of contacts, conducting interviews, evaluating contacts, determining those who are eligible for IPT and ensuring treatment is started on all who are confirmed with TB.

District Information Officer

- Ensure data collection, collation, and analysis for the response, investigation and management of the outbreak
- Disseminate data for prompt and appropriate response, to all users.
- Conduct systematic monitoring and evaluation of the response plans and provide feedback
- Maintain communication with district coordinator and management team

Health Promotion

- Develop and distribute Information, Education and Communication [IEC] materials, e.g. poster, pamphlets and audio-visuals, for increasing public awareness in the all relevant settings
- Increase public awareness through electronic media, television, radio, and internet
- Develop active community participation strategies such as community dialogues, and ensure community involvement
- Mobilise communities

District management team

- Build consensus with province and other technical partners regarding the outbreak response
- Establish accountable systems of communication, evaluation, response and tracking of TB patients and contacts
- Appoint a communication officer
- Ensure the implementation of the response plan, infection control and education of communities and affected groups
- Request assistance from province
- Provide a list of available isolation facilities if needed
- Facilitate education and training for community health care workers and other stakeholders such as employers, schools, NGOs
- Mobilise adequate resources for the response plan
- Monitor the response activities

ANNEXURE 5 :
ALCOHOL USE DISORDERS IDENTIFICATION TEST[4]

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The Alcohol Use Disorder Identification Test: Interview Version

Read questions as written. Record answers carefully. Begin the AUDIT by saying " Now I am going to ask you some questions about your use of alcolholic beverages during this past year." Explain what is meant by "alcoholic beverages" by using local examples of beer, wine, vodka, etc. Code answers in terms of "standard drinks". Place the correct asnwer number in the bod at the right.

1. How often do you have a drink containing alcohol?

(0) Never [skip to Qs 9-10]
(1) Monthly or less
(2) 2 to 4 times a month
(3) 2 to 3 times a week
(4) 4 or more times a week

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
(0) 1 or 2
(1) 3 or 4
(2) 5 or 6
(3) 7,8 or 9
(4) 10 or more

3. How often do you have six or more drinks on one occasion?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily
Skip to Questions 9 and 10 if total Score for Questions 2 and 3 = 0

4. How often during the last year ave you found that you were not able to stop drinking once you had started?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

5. How often during the last year have you failed to do what was normally expected from you because of drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

7. How often during the last year have you had a feeling of guilt or remorse after drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

8. How often during the last year have you been unable to remember what hapened the night before because you had been drinking?
(0) Never
(1) Less than monthly
(2) Monthly
(3) Weekly
(4) Daily or almost daily

9. Have you or someone else been injured as a result of your drinking?
(0) No
(2) Yes, but not in the last year
(4) Yes, during the last year

10. Has a relative or friend or a doctor or another health worket been concerned about your drinking or suggested you cut down?
(0) No
(2) Yes, but not in the last year
(4) Yes, during the last year

Record total of specific items here

If total is greater than recommended cut-off, consult User's Manual

INTERPREATION OF AUDIT SCORES
Scores between 8 and 13: simple advice focused on the reduction of hazardous drinking.
Scores between 16 and 19: brief counselling and continued monitoring
Scores or 20 or above: further diagnostic evaluation for alchol dependence

[4]The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Care, 2nd Edition. WHO, Geneva. 2001

ANNEXURE 6:
TB CONTACT NOTIFICATION FORM

TB CONTACT NOTIFICATION FORM

Name of Health Facility:	Telephone No.:
Address:	
Name of health care worker completing this form:	
Patient name (index case):	Date of issue:
TB Registration number:	Date of Birth/ Age:

Please note that the person presenting this form has been in close contact with the above patient who has been diagnosed with:

	Xpert positive, smear positive Rifampicin susceptible pulmonary TB
	Xpert positive, culture positive Rifampicin susceptible pulmonary TB
	Xpert positive, Rifampicin resistant pulmonary TB

Please screen this person for TB and perform appropriate tests if indicated.

Signature:	Date:

Please send this slip back to the issuing facility as soon as possible

Name of reporting health facility:	Telephone No:
Name of person completing the form:	
Patient name:	Date of reporting:

Screening results	Positive	Negative		
Test conducted	Xpert	Smear	Culture	LPA
Diagnosis	TB	RR-TB	MDR-TB	
Treatment given	Yes	No		
Isoniazid preventive therapy given	Yes	No		

Treatment start date:	Signature:

ANNEXURE 7:
TB SCREENING TOOL

TB SYMPTOM SCREENING TOOL FOR ADULTS AND CHILDREN

PATIENT DETAILS

Surname:	First Name:
Physical Address:	Age:
Telephone Number:	Patient folder Number:

MEDICAL HISTORY

Close contact of a person with infectious TB:	Yes	No	Unknown	(Tick √)
Type of index patient:	DS-TB	Rif Resistant TB	MDR-TB or XDR-TB	
Diabetic:	Yes	No	Unknown	
HIV Status:	Positive	Negative	Unknown	
Other: (Specify)				

TB SYMPTOM SCREEN

1. ADULTS

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more OR of any duration if HIV positive		
Persistent fever of more than two weeks		
Unexplained weight loss >1.5kg in a month		
Drenching night sweats		

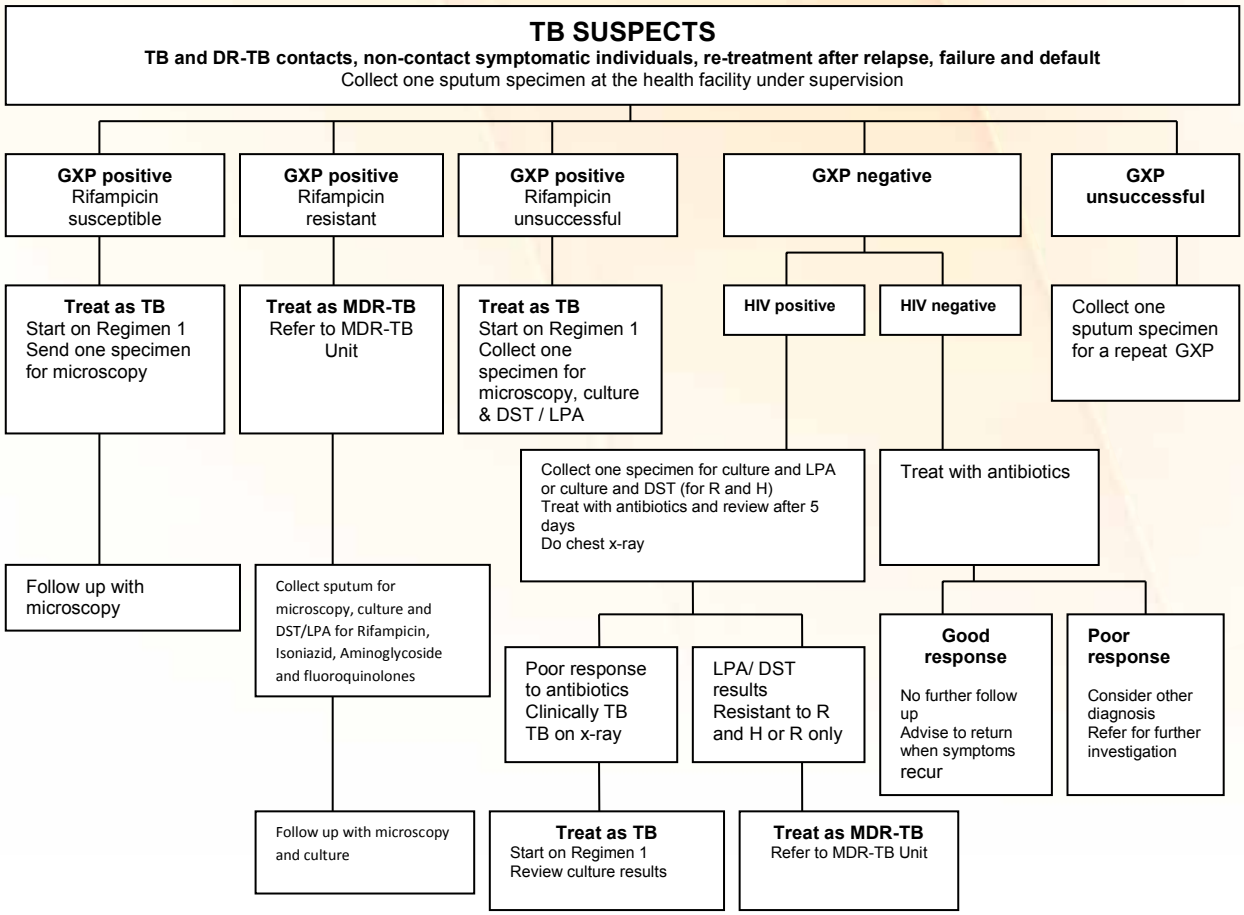
2. CHILDREN

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more which is not improving on treatment		
Persistent fever of more than two weeks		
Documented weight loss/ failure to thrive (check Road to Health Card)		
Fatigue (less playful/ always tired)		

If "Yes" to one or more of these questions, consider TB.
If the patient is coughing, collect sputum specimen and send it for Xpert testing.
If the patient is not coughing but has the other symptoms, clinically assess the patient or refer for further investigation.

Date of last TB test:			
Patient referred for assessment and investigation:		Yes	No
Date of referral:	Facility name:		
Name:	Date:		

ANNEXURE 8:
XPERT DIAGNOSTIC ALGORITHM



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