MINISTRY OF HEALTH AND SOCIAL WELFARE

NATIONAL LEPROSY/TB CONTROL PROGRAMME

NATIONAL GUIDELINES FOR THE MANAGEMENT OF TUBERCULOSIS 2013-2017

THIRD EDITION: REVISED OCTOBER 2012

Preface

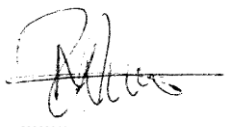
The revised manual of the National TB and Leprosy Programme under the ministry of health which comprises technical and operational guidelines is an update of the second edition. The update was considered necessary in recognition of the following:

- The increased number of stakeholders involved in tuberculosis (**TB**) and leprosy control activities which now include clinicians, public health workers, trainers and health planners

- The interaction between TB and HIV/AIDS which has resulted in increasing numbers of TB and a changed clinical picture which call for a change in the management of these patients. Control of TB will only be achieved through control of HIV/AIDS and vice versa

- The importance of addressing childhood TB in the population
- Addressing the emerging Multi Drug resistant TB (**MDR-TB**) and the
- Urgent need to institutionalize TB infection control in the health care facilities to avoid nosocomial spread and ensure protection of the health workers

These guidelines include information gathered from various stakeholders. In particular, crucial clinical information relevant to The Gambia was gathered and adopted from practising consultant physicians and clinicians on the ground.
The primary users of this manual will be health workers (Doctors, Nurses LTIs, Nurse tutors/Health Planners and RLTCOs) at the operational level for the day to day management of TB patients. The technical staff at the national and regional levels will be responsible for ensuring that these guidelines in the manual are followed by all health workers through orientation, training and supervision. It is my sincere hope that these guidelines will provide the needed guidance in the management and control of TB in The Gambia.
Appreciation goes to all the people who contributed directly and indirectly to the revision of this document.



Dr. Makie Taal
Permanent Secretary
Ministry of Health & Social Welfare
Of The Republic of The

Acknowledgement

For the development of these guidelines, we acknowledge using WHO TB/HIV Clinical Manual, The Gambia NLTP Manual second Edition, and NAS guidelines on Anti-retroviral Therapy in The Gambia and TB Guidelines of Namibia as model guideline. We wish to thank **Dr. Obasanya (Senior TB Consultant - Nigeria)** for his contribution to building up the guidelines. We also wish to thank the following participants who contributed to the development of the TB guidelines.

1. Dr. Adama Demba - Director of Health Services
2. Mrs. Marget Gomez - CNO
3. Mr. Dawda Ceesay - DPI
4. Mrs. Isatou Jallow - NPHL
5. Dr. Ahmet Secka - Clinician
6. Dr. Sillah - MRC
7. Mr. Abdoulie Bah - HMIS
8. Mrs. Jarrai Daffeh - Child's Fund The Gambia
9. Mrs. Awa Sayang - NAS
10. Mr. Alieu Jammeh - NACP
11. Mrs. Fatou Jah Sowe - NPS
12. Mr. Adama Jallow - NLTP
13. Mr. Musa B. Jallow - NLTP
14. Mr. Kejaw Saidykhan - NLTP
15. Mr. Kebba Sanneh - NLTP
16. Mr. Saikou Ceesay - NLTP
17. Mr. Sheriffe Badjie - HEP
18. Mr. Alpha Bah - WHO
19. Mr. Sarjo Sonko - LTI – Brikama TB Clinic
20. Mr. Micheal Sambou - RLTCO – Western (Region 1)
21. Mr. Kebba Ceesay - RLTCO- Banjulinding TB Clinic
22. Mr. Yerro Bah - Manager IMCI
23. Mrs. Rohey Njie - HEP

Mr. Adama Jallow

Manager- NLTP

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Acronyms

ACSM	Advocacy, Communication & Social Mobilization
AFB	Acid-Fast Bacilli
AIDS	Acquired Immune-deficiency Syndrome
ART	Anti-Retroviral Therapy
ARV	Anti-Retroviral
CAT	Category of regimen (abbreviation)
CB-DOTS	Community Based-Directly Observed Treatment
CBO	Community-Based Organization
CCF	Chronic Cardiac Failure
CDC	Centre for Disease Control and Prevention, Atlanta, USA
CMS	Central Medical Stores
CPT	Co-trimoxazole Preventive Therapy
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment - Short course (WHO Strategy)
DST	Drug Susceptibility Testing
DTC	District TB Coordinator
FDC	Fixed-Dose Combination
GFATM	Global Fund to fight AIDS, TB and Malaria
HBC	Home-based Care
HIV	Human Immune-deficiency Virus
HF	Health Facility
HRD	Human Resource Development
HSR	Health Systems Research
IEC	Information, Education and Communication
IPT	Isoniazid Preventive Therapy
IUATLD	International Union Against Tuberculosis and Lung Diseases
KAP	Knowledge, attitude, practices
KNCV	Royal Netherlands Tuberculosis Association
MDR-TB	Multidrug Resistant TB
MIS	Management Information Systems
NACP	National AIDS Control Programme
NGO	Non-Governmental Organization
NMP	National Malaria Programme
NLTP	National Leprosy and TB Control Programme
NHLS	National Health Laboratory Services
OI	Opportunistic Infection
OPD	Out Patient Department
OR	Operational research
PHC	Primary Health Care
PLHIV	People Living With HIV and AIDS
PCP	Pneumocystis Pneumonia
PTB	Pulmonary Tuberculosis
QA	Quality Assurance
RHMT	Regional Health Management Team

STI	Sexually Transmitted Infection
TB	Tuberculosis
TB/HIV	Tuberculosis and HIV Co-infection
TB-IPT	Isoniazid Preventive Therapy for Tuberculosis
TOT	Training of Trainers
UNION	Short name for IUATLD (See above)
WHO	World Health Organization

1 Background information

1.1 Tuberculosis in The Gambia

There have been considerable changes in the epidemiological situation of tuberculosis in The Gambia. For the past years in relation to tuberculosis case detection, the number of cases (all forms) increased from 1812 in 2006 to 2249 in 2011, while the number of new smear-positive cases increased from 1209 cases in 2006 to 1375 in 2011 (NLTP case notification report 2006-2011). On the other hand, 90% of the 2010 cohort of smear-positive TB cases was successfully treated.

These remarkable gains can be attributed to several factors, which include the progressive nationwide expansion of diagnostic and treatment facilities from 11 in 2006 to 32 in 2011, sensitization of communities, and training of health care workers in TB control.

1.2 HIV/AIDS in The Gambia

In The Gambia, like in the neighboring countries, two types of HIV are prevalent, HIV1 and HIV2, but the prevalence of the latter is slightly decreasing over the last decade. The prevalence of HIV1 and HIV2 in the adult population was 1.7 % and 0.07 % respectively in 2011 (NSS, 2011) .

ART was introduced in 2004 and at the end of 2011 more than 2,891 HIV-positive patients were on antiretroviral treatment, which is coordinated in 10 ART-clinics.

1.3 TB/HIV co-infection in The Gambia

For TB patients, provider-initiated HIV counseling and testing (PICT) has been introduced since 2006. In 2011 93% of registered TB patients were counseled and tested for HIV and among the HIV-positive TB patients 93 % were taking Cotrimoxazole Preventive Therapy (CPT), while 46 % were on ART in 2010 according to NLTP data. By the end of December 2011, a total number of 10,373 People Living with HIV (PLHIV) were screened for TB.

2. The National Leprosy and Tuberculosis Control Programme

2.1 Structure of NLTP

Since the inception of the National Leprosy and TB Control programme attempts have been made at decentralization and integration of the TB activities into the general public health services. At the service level, TB programme activities are fully integrated. Nurses and doctors undertake the core activities of diagnosis and treatment of tuberculosis. TB care services are available free of charge in the public sector. Structurally, NLTP activities are implemented through a decentralized system at national, regional, facility and community levels.

2.2 Strategy for Tuberculosis Control

The goal of the NLTP is to reduce the burden of Tuberculosis in line with the millennium Development Goals (MDG) and the StopTB Partnership targets.

This is to reduce transmission, morbidity and mortality of TB to a level that it is no longer a public health problem in The Gambia.

2.3 Strategy to Control Tuberculosis

The NTLP strategy to control TB is outlined in the new Strategic Plan (2013- 2017) are in line with the new STOP TB strategy recommended by WHO. It is based on the following elements:

1. Pursuing high quality DOTS expansion and enhancement
    i. Political commitment with increased and sustained financing
    ii. Case detection through quality assured bacteriology
    iii. Standardized treatment, with supervision and patient support
    iv. Effective drug supply and management system
    v. Monitoring & evaluation system, and impact measurement

2. Addressing TB/HIV, MDR-TB and other challenges
3. Contributing to health system strengthening
4. Involving all care providers
5. Engaging people with TB and affected communities
6. Enabling and promoting operational research

3. Diagnosing Tuberculosis (Adults)

3.1 What is Tuberculosis

Tuberculosis (TB) is a communicable disease caused by a type of bacteria known as *Mycobacterium tuberculosis* (commonly referred to as TB bacilli). The bacilli usually attack the lungs, causing pulmonary TB (PTB). TB bacteria can also attack other parts of the body such as the spine, lymph nodes, brain and kidneys; this is known as extra-pulmonary TB (EPTB).

3.2 Transmission

When individuals with infectious tuberculosis cough, sneeze, talk or spit, they propel TB bacilli into the air. Transmission is more intense in crowded, poorly ventilated spaces with little ambient sunlight as it increases the likelihood of inhalation of infectious TB bacilli present in the air. If not treated, a person with active pulmonary TB disease will infect, on average, between 10 and 20 people every year. Persons infected by *M. tuberculosis* but who have no symptoms of TB disease have what is known as latent TB infection. After infection, TB bacilli can lie dormant in the body for many years. If the immune system is somehow compromised as in the case of HIV infection, malnutrition or other conditions the TB bacilli can cause active disease. Many factors influence the progression from infection to disease. The most important is HIV infection. Other factors include age, diabetes and cancer

3.3 Tuberculosis suspect

A TB suspect is defined as any person who has productive cough or fever for more than 2 weeks with or without the following:

- Respiratory symptoms (shortness of breath, chest pains, haemoptysis); or
- Constitutional symptoms (loss of appetite, weight loss > 5% of baseline weight, night sweats).

However, among PLHIV, a TB suspect is persons with any current symptom of any duration as follows

- Cough
- Fever
- Weight loss or
- Night sweats

Symptoms that may indicate involvement of TB in the lungs include coughing up blood or sputum and pain in the chest.

Symptoms or signs due to EPTB depend on the site involved. Regardless of the site of disease, there are usually constitutional symptoms present such as fever, night sweats and weight loss.

Table 3.1: Symptoms of Tuberculosis Disease

Pulmonary	**General: Pulmonary and Extra-pulmonary**	**Extra-pulmonary**
▪ Coughing ▪ Coughing up sputum or blood ▪ Pain in the chest when breathing or coughing	▪ Chills ▪ Fever ▪ Night sweats ▪ Loss of appetite ▪ Weight loss ▪ Weakness or easy fatigability ▪ Malaise (a feeling of general discomfort or illness)	The symptoms depend on part of body affected by tuberculosis (TB) disease: ▪ TB of the spine may cause pain in the back. ▪ TB of the kidney may cause blood in the urine. ▪ Meningeal TB may cause headaches or psychiatric symptoms. ▪ Lymphatic TB may cause swollen and tender lymph nodes, often at the base of the neck.

3.4 Approach to Tuberculosis diagnosis

Early identification and treatment of TB cases is important for TB control. Direct sputum smear examination should be done on all tuberculosis suspects, especially among PLHIV having TB symptoms of *any* duration and HIV-negative suspects with cough lasting two weeks or more.

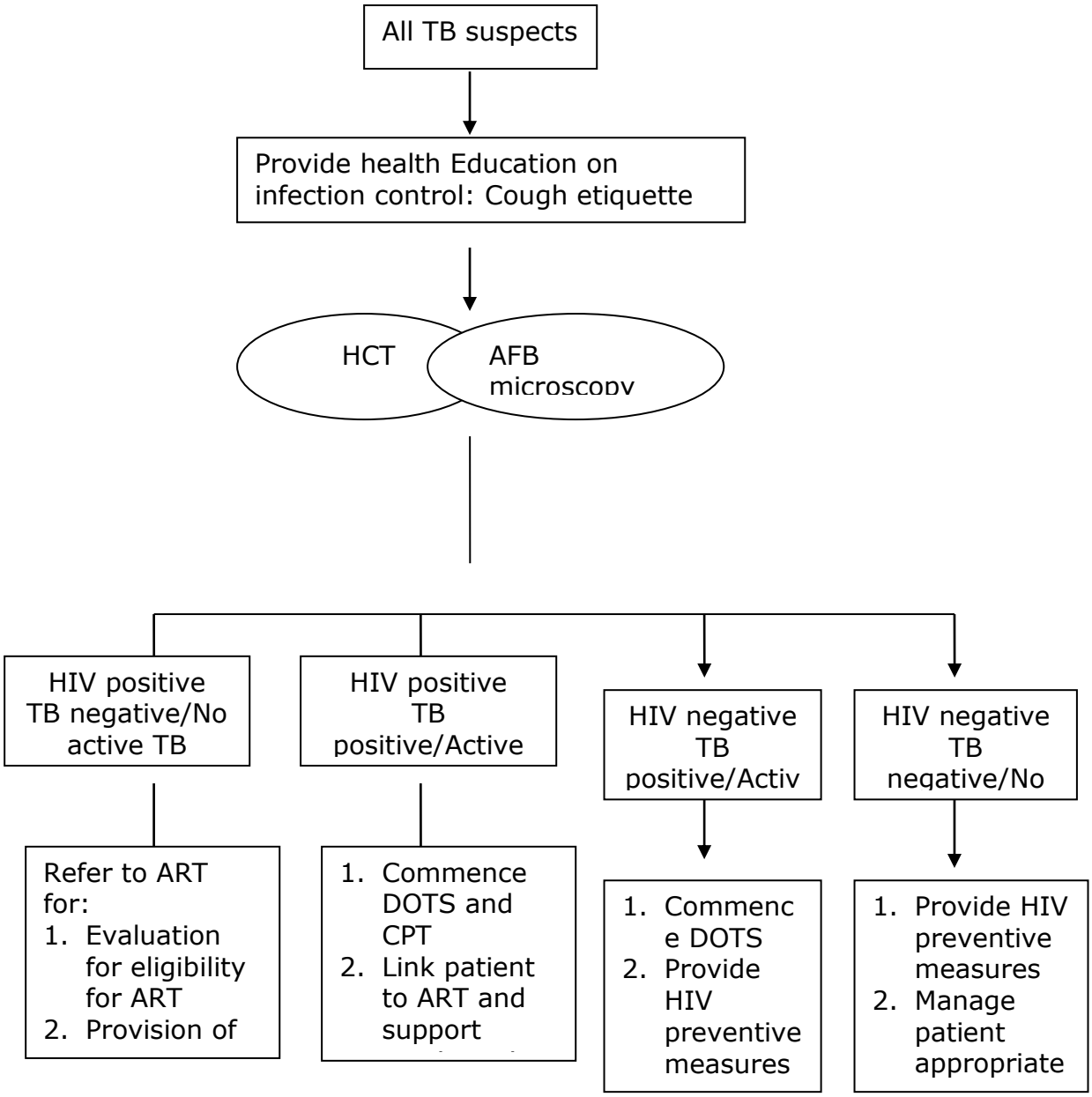
In high-risk institutions where people live under crowded conditions, such as prisons, patients coughing for more than one week should submit sputum for smear microscopy. If the results at one week are negative and symptoms persist after a course of empiric antibiotic treatment, the test should be repeated at 3 weeks.

To improve TB diagnosis, the NLTP will introduce new, rapid molecular tests (Xpert MTB/RIF) and MGIT liquid culture that detect TB bacilli with greater sensitivity than traditional laboratory methods. Xpert MTB/RIF can detect TB bacilli as well as the presence of rifampicin resistant strains in a few hours.

Tuberculosis cases are most frequently found among the following:

- Patients who present themselves on their own initiative at a health facility with symptoms suggesting tuberculosis;
- Those (especially children and young adults) living in the same household with smear-positive patients;
- Those infected with HIV
- Those found to have an abnormality that has the appearance of tuberculosis when a chest radiograph has been taken for clinical investigation of a sick patient

Figure 3.1 Approach for management of TB Suspects



3.5 Clinical presentation

Active TB disease causes a variety of symptoms depending on the anatomical site(s) involved. In settings with high HIV prevalence, up to two-thirds of TB patients may present with symptoms suggestive of extra-pulmonary disease or *both* pulmonary and extra-pulmonary disease.

Patients should be suspected of TB and undergo a thorough investigation for TB if:

- They are children who have been in close contact with a known TB patient;
- They are HIV positive; or
- They were treated for TB in the past.

Pulmonary tuberculosis (PTB)

In the early stages of the disease, symptoms are non-specific. Symptoms classically consist of fever, weight loss, loss of appetite, night sweats, general malaise and weakness. Absence of fever or cough does not exclude a diagnosis of tuberculosis, particularly in patients with HIV or malnutrition. Many patients may have no abnormalities detected on chest auscultation whereas others may have crackles overlying the involved areas.

Extra-pulmonary tuberculosis (EPTB)

EPTB may affect any organ outside of the lungs. Commonly involved sites include: the pleura, lymph nodes, meninges, bones and joints, spine, genitourinary tract, peritoneum and pericardium.

Any person suspected of having extra-pulmonary TB should be referred to a Medical Officer where appropriate samples and diagnostic methods will be used.

3.6 Laboratory Diagnosis of pulmonary Tuberculosis

3.6.1 Specimen for diagnosing tuberculosis

Whenever possible, bacteriologic confirmation of TB by one of the laboratory methods described below should be used to make a definitive diagnosis of TB disease. Bacteriology refers to using smear, culture or newer methods to definitively identify *M. tuberculosis* in a clinical sample from a TB suspect. Smear microscopy and culture remain the cornerstones of bacteriologic confirmation of TB in The Gambia.

It is important to note that the absence of bacteriologic confirmation of TB should *not* delay treatment of a TB suspect with a history and clinical findings **compatible** with TB disease, especially in seriously ill patients, children and People Living with HIV/AIDS. In some instances and particularly in children, a culture or molecular test may be negative even though the patient clinically has TB disease (on the basis of clinical, radiographic and histopathology findings or response to anti-TB treatment).

The laboratory diagnosis of TB begins with the collection of a quality clinical specimen. In the majority of cases this is a sputum specimen.

3.6.2 Sputum collection

Patients and guardians should be counseled and advised properly on how to produce quality sputum specimens. To minimise the number of patient visits, only two sputum specimens should be collected using the 'spot-morning' approach. The first specimen should be collected at the time when the patient first presents to the clinic. During the patient's visit, a second labeled sputum container should be given to the patient and/ or guardian so that his or her sputum can be collected the next morning.

Before collecting sputum

- Patients should be well informed about the diagnostic process and the reason for collecting sputum.
- Sputum collection should be done in the open air (or ventilated room) away from other people to avoid infecting them.
- Patients should clean their mouths if they have been eating.
- A health worker should demonstrate how to cough and how to open and close the sputum container.
- The laboratory request form should be filled out accurately and completely.
- Clearly label the sputum container with the patient's name and the date of collection. Label the container itself, not the lid.
- Make sure that the patient's details have been recorded in the TB suspect register.

How to collect a quality sputum specimen

- Tell the patient that the best specimens come from deep inside the lungs after coughing, not from saliva.
- Demonstrate how to cough deeply.
- Ensure that no one is standing in front of patient producing sputum.
- Instruct the patient to:
    a. Inhale deeply 2 to 3 times and to breathe out hard each time,
    b. Cough deeply from the chest,
    c. Place the open container close to the mouth to collect the sputum, and
    d. Screw the lid tightly.
- Avoid contaminating the outside of the sputum container with sputum. If the outside is contaminated, discard the container and repeat the collection with a fresh container.
- The volume of the sputum should be about 3 to 5 ml.

After collecting a sputum specimen

A. Double check to ensure that the container is labeled properly,

B. Ensure that the container is firmly closed, and

C. Wash your hands with soap and clean water.

- The two sputum specimens should be sent to a microscopy site *within 24 hours*.
- Store sputum specimens for culture, preferably in a refrigerator or in a cool, safe and dark place.
- Sputum specimens for culture should be sent to the laboratory *within 4 days.*
- Do not use laboratory request forms for wrapping specimens.

Who should collect sputum specimens?

- It is the responsibility of health workers and Village Health Workers to refer all TB suspects to the lab for sputum collection.
- The laboratory personnel is responsible for the collection of sputum
- TB suspects received at the OPD or TB clinic should be referred to the lab for screening using sputum request form
- For in-patients, the ward nurse should collect early morning sputum samples for submission to the laboratory.
- At health centre and community levels, Community Health Nurse (CHN) and Village Health Workers should follow up with TB suspects to ensure sputum specimens are collected.
- Should the patient not return after submission of the first spot specimen; the CHN, Village Health Workers or LTI must follow up the patient immediately.

3.6.3 Transportation of sputum specimen

- Sputum specimens should be sent to the laboratory as soon as possible to ensure examination is done within 48hours of collection.
- .
- All samples should be properly labeled. Ensure that the container is firmly closed
- If samples require further investigations it should be packed carefully, preferably in a transport box.
- Make sure that every specimen is accompanied with a laboratory request form.
- A cold chain should be maintained throughout the transportation process, especially when sending samples for culture.
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- **Sputum microscopy can be done by Ziehl-Nielsen conventional light microscopy or by fluorescent microscopy.**
- **Laboratory personnel should perform sputum examination the same day samples are submitted, aiming to return a result to the patient within 48 hours.**

3.6.4 Sputum microscopy

- Sputum smear microscopy is the primary test for the diagnosis of pulmonary tuberculosis (PTB).
- Diagnosis of TB by smear microscopy is made by visual identification of acid-fast (AFB) or fluorescent bacilli under direct examination of a stained sample by conventional light or fluorescent microscopy, respectively.
- Fluorescent microscopy is a new way to detect TB bacilli using a specialised microscope. It is a more sensitive and less-time consuming technique than

traditional light microscopy.

- Laboratory personnel report results based on the number of TB bacilli seen when evaluating areas visualised under the microscope called “fields” (see Table 3.2).

Table 3.2: Reporting laboratory results

Result reported	**Interpretation**
Negative	No bacilli seen in 100 fields
“Scanty” or actual number counted	1 to 9 bacilli seen (either acid-fast or fluorescent) in 100 fields*
1+	10 to 99 bacilli seen (either acid-fast or fluorescent) in 100 fields
2+	1 to 10 bacilli seen (either acid-fast or fluorescent) per 1 field
3+	> 10 bacilli seen (either acid-fast or fluorescent) per 1 field

All smear-positive (including scanty) results should be recorded in red ink in the Tuberculosis Laboratory Register.

3.6.5 Interpretations of smear results

3.6.5.1 Smear positive pulmonary TB

Identifying just one positive sputum smear with even one bacilli detected at the start of treatment meets criteria for classifying a patient as a “smear-positive” case. Smear-positive patients are the most infectious and most likely to transmit the disease to people in their surroundings; as such, they have historically been the primary focus of infection control measures and contact tracing efforts.

3.6.5.2 Smear negative pulmonary TB

A patient is a smear-negative TB case if one of the following criteria is met:

- Negative smear on microscopy, an inconclusive chest x-ray but a decision by a clinician to treat with a full course of anti-TB drugs based on a positive HIV test or clinical evidence of HIV and a clinical presentation compatible with TB.

- Negative smear on microscopy and a decision by a clinician to treat with a full course of anti-TB drugs based on abnormalities on chest x-ray consistent with active pulmonary TB plus one of the following:
    - Positive HIV test or strong clinical evidence of HIV infection, OR
    - If HIV-negative, no improvement with a course of broad-spectrum antibiotics.

It is important to identify smear negative PTB especially in persons living with HIV, because

the mortality is high. For this reason, aggressive early TB treatment and close follow-up of HIV-positive TB suspects, especially those who are seriously ill, is critical to prevent unnecessary TB deaths.

- A sputum smear result is positive if at least one tubercle bacillus (acid-fast OR fluorescent) is detected on one or more sputum smears.
- The patient should be registered as a smear-positive case and should be started on TB treatment immediately.
- If both sputum smears are negative, the patient should be investigated further for TB. The patient should receive a thorough clinical evaluation and undergo further testing by chest x-ray and/or Xpert MTB/RIF. Please refer to the diagnostic algorithm for details.

3.6.6 Chest X-ray

Chest x-ray findings especially in patients with a negative sputum smear should be correlated with clinical findings, history and physical examination. Chest x-ray appearances alone do not always help diagnose PTB. In 10 to 20% of HIV-positive patients with PTB, the chest x-ray is not suggestive, particularly with advance stage infection. A normal x-ray does not rule out TB in a patient with compatible symptoms and clinical findings. Patients with a normal x-ray who remain symptomatic should be referred to a clinician for further investigations.

Classic radiographic findings suggestive of TB, particularly in patients who are not immune compromised, include:

- Upper lobe infiltrates
- Cavitary lesions
- Hilar and/or para-tracheal lymphadenopathy

In patients with primary PTB and HIV infection, the x-ray findings can be quite different:

- Lower lobe infiltrates
- A miliary or “scattered seed” like pattern

All persons with chest radiographic findings suggestive of TB should submit sputum specimens for microbiological examination

3.6.7 Tuberculin test

A tuberculin skin test is sometimes used by health care workers to help in the diagnosis of tuberculosis. The response to the intradermal injection of tuberculin is read 48–72 hours later, requiring the patient to revisit the clinic after the injection was administered. The interpretation of a test result is often very difficult, as a positive test may be caused by conditions other than tuberculosis and a negative test does not always rule out tuberculosis. A significant reaction to the test indicates the presence of infection but cannot indicate whether or not the patient has the disease. Many patients with advanced immunosuppression related to HIV will fail to react to the test even when they have the disease. Therefore, tuberculin skin test cannot be used as a single diagnostic test for adults.

3.6.8 Xpert MTB/Rif investigation

Xpert MTB/RIF is a new rapid molecular test for detecting TB in sputum. Xpert MTB/RIF simultaneously tests for drug resistance to rifampicin, enabling earlier diagnosis and treatment initiation for MDR-TB patients. Testing with Xpert MTB/RIF requires only one sputum specimen and can detect both TB and rifampicin- resistance in less than 2 hours.

The NLTP has prioritised the following patients for Xpert MTB/ RIF testing:

- All smear-negative TB suspects (PLHIV)
- All TB cases who fail treatment
- All confirmed retreatment cases and MDR-TB suspects
- Contacts of MDR-TB cases

Despite the introduction of Xpert testing, sputum microscopy remains the backbone of the TB diagnostic network. Along with culture and drug susceptibility testing (DST) it also continues to be the method of choice for monitoring patient response to anti-TB therapy.

3.7 Laboratory diagnosis of Extra-pulmonary Tuberculosis

Since Extra-pulmonary tuberculosis (EPTB) refers to a case of TB (defined above) involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges. Diagnosis is based on at least one specimen with confirmed *M. tuberculosis* or histological or strong clinical evidence consistent with active EPTB, followed by a decision by a clinician to treat with a full course of tuberculosis chemotherapy.

All patients suspected of EPTB should be offered HIV counseling and testing. If HIV positive, they should start co-trimoxazole preventive therapy (CPT) immediately and antiretroviral therapy (ART) according to national guidelines

Table 3.3: Specimens for diagnosis of Tuberculosis

Suspected Diagnosis	Specimen Needed
Pulmonary or laryngeal tuberculosis (TB)	Sputum (phlegm from deep in the lungs) samples for smear and culture examination. If a diagnosis of pulmonary TB cannot be established from sputum smear, other procedures may be necessary, including Xpert MTB/Rif bronchoscopy, and gastric aspiration in children.
Extra-pulmonary TB	Depending on the anatomical site, other clinical specimens are necessary, such as: ▪ Urine ▪ Cerebrospinal fluid ▪ Pleural fluid ▪ Pus or other aspirated fluid ▪ Biopsy specimens ▪ Blood (heparinized)

4 Treatment of Tuberculosis

4.1 Case definitions and Category for Treatment of Tuberculosis

It is crucial to define TB cases properly for accurate patient registration and selection of treatment regimens. This will in turn aid standardisation of data collection and cohort analysis for treatment outcomes. The TB case definitions below are based on the level of certainty of the diagnosis and on whether or not laboratory confirmation is available.

4.1.1 A Case of TB

A case of TB is:

- A patient with pulmonary symptoms having at least one sputum-smear examination positive for acid-fast bacilli (AFB) by either conventional or fluorescent microscopy;
- A patient with *M. tuberculosis* complex identified from a clinical specimen, either by culture or by a molecular diagnostic method such as Xpert MTB/RIF; **or**
- A patient in whom a health worker or a clinician has diagnosed TB and has decided to treat with a full course of TB treatment.

Cases of TB are also classified according to the:

- Anatomical site of disease,
- Bacteriological results (including drug resistance),
- History of previous treatment, and HIV status.

4.1.2 Anatomical site of disease

In general, recommended treatment regimens are similar, irrespective of the anatomical site of disease. Defining the site is important for recording and reporting purposes and to

identify the more infectious patients—those with pulmonary involvement (who will be further subdivided by smear status).

Pulmonary tuberculosis (PTB)

This is a form of tuberculosis that involves the lung tissues. Miliary tuberculosis is classified as pulmonary TB because there are lesions in the lungs as well. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of *pulmonary* TB.

Extra-pulmonary tuberculosis (EPTB)

This type of TB involves one or more organs other than the lungs, for example, the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and/ or meninges.

Both intra-thoracic tuberculous lymphadenopathy (e.g. involving the mediastinal and/or hilar lymph nodes) and tuberculous pleural effusion, when radiographic abnormalities in the lungs are absent, constitute cases of *extra-pulmonary* TB.

4.1.3 Bacteriological results (including drug resistance)

Bacteriological status refers to the detection of *M. tuberculosis* by smear, culture or molecular methods, and to the detection of drug sensitive and drug resistant cases. Any case with a positive bacteriological result (microscopy, culture or molecular method) is defined as a "bacteriological positive TB case". If the bacteriological tests are all negative or not done the case is defined as a "bacteriological negative TB case". TB cases are sub-classified as "smear-positive" or "smear-negative", which is useful because it best correlates with infectiousness.

- Smear-positive pulmonary TB: Patient with at least one sputum smear-positive sample (at least one AFB is found in at least one sputum sample: scanty results are considered as positive).
- Smear-negative pulmonary TB: Pulmonary TB that are negative for AFB and for whom a clinician prescribes anti-TB treatment.

4.1.4 History of previous treatment, and HIV status.

TB cases can also be defined according to whether or not a patient has a new infection or has previously received TB treatment. It is important to identify previously treated patients because they are at increased risk of having drug-resistant TB. At the start of treatment specimens for culture and DST should be obtained from all previously treated patients.

Table 4.1: Category of patients based on history of previous treatment

Category	Definition
New	A patient who has never been treated previously for TB or who has taken TB treatment for less than one month. This could be a PTB (smear-positive or smear-negative) or EPTB case.

Previously treated	**Relapse**	A patient who presents positive bacteriologically (by smear, culture or molecular method) after previously undergoing TB treatment with a successful outcome (cured or completed treatment).
	Failure	A patient whose sputum smear or culture is positive at 5 months or later whilst on anti-TB chemotherapy. (Of note, also included in this definition are patients found to have MDR-TB at any point during treatment, regardless of whether they were initially smear-negative or -positive).
	Treatment after default	A bacteriologically positive patient who is started on treatment after previous treatment was interrupted for at least 2 consecutive months (default).
	Transfer-in	A patient who has been transferred from another treatment unit to continue treatment.
	Other	All cases that do not fit the above definitions, such as patients: For whom it is not known whether they have been previously treated; Who were previously treated but with unknown outcome of that previous treatment; and/or Who have returned to treatment with smear-negative pulmonary TB or bacteriologically negative EPTB.

***Note*. Any person given treatment for TB should be recorded as a case. Incomplete "trial" TB treatment should not be given as a method for diagnosis.**

4.2 Treatment of Tuberculosis in Adults

4.2.1 Aims of treatment

The aims of treatment of tuberculosis are:

- To cure the patient and restore quality of life and productivity;
- To prevent death from active TB or its late effects;
- To prevent relapse of TB;
- To reduce transmission of TB to others;
- To prevent the development and transmission of drug resistance.

4.2.2 Directly-observed treatment (DOT)

The treatment supervisor watches the patient swallow the tablets throughout the whole course of treatment. DOT ensures that the TB patient takes the right drugs, in the right doses at the right times. Supervisors or "treatment supporters," can be health workers, volunteers, and trained members of the community or guardians.

- A patient-centered approach with proper communication between the patient and treatment supporter promotes patient education, good adherence and early identification of challenges with treatment (including side effects and clinical worsening).
- All treatment supporters should be chosen together with and should be acceptable to the patient.
- The need for good adherence and follow-up should be reinforced at all times.
- Patients should be reminded about the duration of treatment and common side effects.
- DOT allows the prompt detection and management of adverse drug reactions and clinical worsening of TB.

4.2.3 Treatment of drug susceptible Tuberculosis (New)

4.2.3.1 Treatment regimen for new PTB patient

Susceptible TB is treated with first-line drugs: Rifampicin (R), Isoniazid (H), Ethambutol (E), and Pyrazinamide (Z). These drugs (RHZE) are available in fixed dose combination (FDC) tablet. Streptomycin (S) is a first- line injectable drug used in the retreatment regimen and for TB meningitis**.**

Table 4.2: Standard regimen for new TB patients (except TB meningitis)

Intensive Phase	Continuation Phase
RHZE daily for 2 months	RH three times a week 150/150 for 4 months

Patients should not be admitted in the ward or hospital for administration of TB drugs except where they are too sick or unable to walk. TB drugs should be provided on ambulatory basis in all facilities.

Table 4.3: Regimen and dosages of anti-tuberculosis drugs for new PTB patients (adult)

Weight Bands	**Number of Tablets**	
	Intensive Phase (2 months)	**Continuation Phase (4 months)**
	RHZE (150mg+75mg+400mg+275mg)	**RH (150mg/150mg)**
25 – 37 kg	2	2
38 – 54 kg	3	3
55 – 70 kg	4	4
>70 kg	5	5

- **Patient weight should be monitored each month, and doses adjusted if weight changes.**
- **If the patient continues to lose weight while on treatment, they should undergo a detailed review by a clinician.**
- **New smear-positive PTB patients treated with first- line drugs should submit a sputum sample for smear microscopy at completion of the intensive phase.**
- **Xpert MTB/RIF should not be used to monitor response to treatment in TB patients.**

4.2.3.2 Sputum monitoring by smear microscopy in new PTB patients

New smear-positive cases should submit sputum at 2 months, 5 months and 6 months.

Table 4.4: Sputum monitoring in new PTB patients

Months of treatment					
1	**2**	**3**	**4**	**5**	**6**
	♦ If smear-positive, repeat in month 3	♦ If smear positive, obtain sample for Xpert MTB/RIF, culture and DST		♦ If smear-positive, obtain sample for Xpert MTB/RIF culture and DST	♦ If smear-positive, obtain sample for Xpert MTB/RIF, culture and DST

Key: ♦ Sputum smear examination

a. Not necessary if the patient was smear-negative at the start of treatment

b. Smear- or culture-positive at month 5 or later is defined as treatment failure and requires: (a) re-registration of the patient as a "Treatment Failure"; (b) change to retreatment regimen and (c) sending sputum for Xpert MTB/RIF.

Note: Patients who have a diagnosis of rifampicin-susceptible TB made by Xpert MTB/RIF should be monitored by sputum smear microscopy at 2, 5 and 6 months into treatment.

A positive sputum smear at the end of the intensive phase may indicate one of the following problems:

- The initial phase was poorly supervised;
- Patient adherence to treatment is inadequate;
- The anti-TB drugs are being under-dosed (as may happen if a patient gains weight during the intensive phase);
- There are co-morbid conditions that interfere with treatment response or adherence (e.g., mental illness, ART treatment failure, substance abuse etc.);
- The patient may have drug-resistant TB that is not responding to first-line treatment

At the end of month 2, if sputum examination result is:

- Sputum smear-negative: Start continuation phase of treatment.
- Sputum smear-positive: Intensive phase but repeat sputum smear at the end of month 3.

At the end of month 3 if result is or remain:

- Sputum smear-negative; continue the continuation phase of treatment.
- Sputum smear-positive: switch to continuation phase.

At the end of month 5 if result is:

- Sputum smear-negative: keep on with continuation phase.
- Sputum smear-positive: collect samples and do Xpert MTB/Rif, culture & DST examinations, re-register as Treatment Failure and start on retreatment regimen while awaiting DST results

If Xpert MTB/RIF, culture and DST results show MDR-TB refer for MDR-TB treatment.

4.2.3.3 Tuberculosis meningitis (TBM)

The regimen for TBM is 2SRHZE/10RH; that is, two months of streptomycin plus FDC RHZE given daily under close supervision followed by ten months of daily RH.

Table 4.5: Treatment regimen for patients with tuberculosis meningitis

Weight Bands	**Number of Tablets**	
	Intensive Phase (2 months)	**Continuation Phase (10 months)**
	RHZE (150mg+75mg+400mg+275mg)	**RH (150mg/150mg)**
25 – 37 kg	2	2
38 – 54 kg	3	3
55 – 70 kg	4	4
>70 kg	5	5

Corticosteroids should be given along with anti-TB drugs as they have been shown to significantly reduce the risk of death in patients with TB meningitis (see 6.6).

4.2.4 Treatment regimens for patients previously treated for tuberculosis

4.2.4.1 Regimen for previously treated patients

Previous TB treatment is a strong determinant of drug resistance. It is critical in previously treated patients to detect drug resistance, especially MDR-TB so that an effective drug regimen can be employed as early as possible. First-line drug regimens are not effective against MDR TB strains and can result in mortality and morbidity, amplification of resistance, and further spread of MDR-TB. The following strategy in previously treated patients should be employed:

- The presence of drug-resistance should be determined in all previously treated TB patients at or before the start of treatment.

- Xpert MTB/Rif is the preferred screening method for MDR-TB because of its sensitivity and quick turn-around time. All previously treated patients should submit specimen for Xpert MTB/Rif without necessarily waiting for confirmation of conventional DST.

- When Xpert MTB/Rif results will be delayed (because of transport delays or backlogs):
  - Patients returning after defaulting or relapsing from their first treatment course may receive a retreatment regimen with first-line drugs, 2(RHZE) S/1(RHZE)/5(RHE), while awaiting DST results (culture or Xpert MTB/RIF). When DST becomes available the regimen should be adjusted if resistance is found. If no resistance is found continue 2(RHZE) S/1(RHZE)/5(HRE).

Table 4.6: Retreatment regimen with first-line drugs for patients previously treated for tuberculosis and low-risk for MDR-TB

Intensive Phase	Continuation Phase
SRHZE daily for 2 months, then RHZE for 1 month	RHE daily for 5 months

Note: All medicines should be given under directly observed treatment (DOT) throughout the whole course of treatment.

Table 4.7: Regimen and dosages of anti-tuberculosis drugs for previously treated patients (**Relapses, Failures, RAD and Others)**

Weight Bands	**Number of Tablets**		
	Intensive Phase (3 months)		**Continuation Phase (5 months)**
	RHZE (150mg+75mg+400mg+275mg)	**S (gm)** **Add streptomycin daily in the first 2 months**	**RHE (150mg+75mg+275mg)**
25 – 37 kg	2	0.5 gm.	2
38 – 54 kg	3	0.75 gm.	3
55 – 70 kg	4	1 gm.	4
>70 kg	5	1 gm	5

1. Streptomycin should NOT be given to pregnant women.
2. Patients >45 years should not be given more than 0.75g of streptomycin irrespective of weight

- **The National TB Strategic Plan sets a target of all previously treated patients having access to Xpert MTB/ RIF before beginning treatment. The purpose is to identify MDR-TB as early as possible so that appropriate treatment can be given.**
- **Specimens for culture and drug susceptibility testing (DST) should be obtained from all previously treated TB patients at or before the start of treatment and sent to the Central Reference Laboratory.**
- **In Regions with access to Xpert MTB/RIF, sputum samples should be sent for Xpert MTB/RIF at or immediately before the start of treatment.**

4.2.4.2 Sputum monitoring by smear microscopy for retreatment patients receiving the 8-month regimen

Retreatment patients should submit sputum at 3 months, 5 months and 8 months. If the sputum smear is positive at 3 months, obtain sputum specimen for Xpert MTB/RIF, culture and DST.

Table 4.8: Sputum monitoring of PTB patients receiving the 8-month retreatment regimen with first-line drugs

Months of treatment							
1	**2**	**3**	4	5	6	7	**8**
Intensive phase (2RHZE/1RHZE)			**Continuation phase (RHE)**				
		♦ If smear positive, obtain sample for Xpert MTB/RIF, culture and DST		♦ If smear positive, obtain sample for Xpert MTB/RIF, culture and DST[a]			♦ If smear positive, obtain culture and DST[a]

Key ♦ Sputum smear examination

[a] A positive smear- or culture at month 5 or later (or detection of MDR-TB at any point) is defined as treatment failure and necessitates re-registration. MDR-TB should be strongly suspected in any patient who fails a retreatment regimen.

4.2.5 Use of anti-tuberculosis drugs in special situations

The following special situations require an adjustment of standardised TB regimens.

Pregnancy

- Streptomycin is potentially ototoxic and may cause deafness in babies.
- Streptomycin should not be given in pregnancy.
- Isoniazid, rifampicin, pyrazinamide and ethambutol are safe in pregnancy.
- Pyridoxine supplementation is recommended for all pregnant and breastfeeding women receiving isoniazid.

Oral contraceptives

- Rifampicin reduces the effectiveness of the oral contraceptive pill.
- Health workers should advise patients on TB treatment to use barrier contraception

like male or female condoms while on rifampicin.

Renal impairment and renal failure

- Ethambutol and pyrazinamide are cleared by the kidneys and should be reduced to three times per week.
- Streptomycin should be avoided in patients with renal failure or if it must be used, the frequency should be reduced.

Table 4.9: Recommended dosages in patients with renal failure

Drug	**Dose**	**Normal frequency**	**Frequency in renal failure**
Pyrazinamide (Z)	25 mg/kg	Daily	3x/week
Ethambutol (E)	15 mg/kg	Daily	3x/week
Streptomycin (S	15 mg/kg	Daily	2 – 3x/week

Liver impairment and liver failure

- Isoniazid, rifampicin and pyrazinamide are recognised to be hepatotoxic.
- TB patients with active liver disease (i.e., those with jaundice or ascites) should not receive pyrazinamide or rifampicin.
- They should be given 2 months of streptomycin, isoniazid and ethambutol during the intensive phase of treatment, followed by 10 months of isoniazid and ethambutol.
- If the jaundice is acute and severe, then treat initially with only streptomycin and ethambutol.

Epilepsy

- Rifampicin induces liver enzymes that reduce levels of anticonvulsant medications (phenobarbital and phenytoin) in the blood.
- Increase the dose of the anticonvulsant and monitor the patient closely for increasing seizure frequency.

TB/HIV and taking ART

- Rifampicin induces liver enzymes that reduce levels of nevirapine in the blood.
- All HIV-positive TB patients should initiate an efavirenz- based regimen to minimise

drug interactions with rifampicin.

Refer to Chapter 7 for more information on TB/HIV co-infection.

Corticosteroids and tuberculosis

- Corticosteroids, in conjunction with anti-TB drugs, reduce the risk of death in TB meningitis and TB pericarditis.
- Patients with TB meningitis or TB pericarditis should be given corticosteroids (60mg for adults and 1mg/kg wt. (max 40mg) in children) for an initial period of 21 days followed by tapering off by 25% per week over four weeks.
- Either prednisolone or dexamethasone may be used.

4.3 Managing interruption of treatment

During each visit, the health worker should record and confirm the patient's address, other relevant addresses (such as those of family members) and, if possible, the patient's or a family member's mobile phone number in case the need to contact or track the patient arises. Should a TB patient miss a scheduled appointment, action must be taken within three days of the date the patient was due for his or her scheduled appointment or drug collection. It is the responsibility of the Leprosy/TB Officer (LTI) to ensure a sound default-tracking plan is in place and implemented at district level. The LTI may call upon CHN, community volunteers and/or other health workers to locate a patient who has defaulted.

Table 4.10: Actions to manage interruption of treatment.

Length of interruption	**Do a smear?**	**Result of smear**	**Duration of treatment**	**Treatment**
< 1 month	No	-	-	Continue Rx and prolong to compensate for missed doses
1-2 months	Yes (3 samples)	Negative or EPTB	-	Continue Rx and prolong to compensate for missed doses
		If 1 or more positive	< 5 months	Continue Rx and prolong to compensate for missed doses
			>5 months	Cat 1: Start Cat 2 and send sample for rapid DST
				Cat 2: Send sample for rapid DST and continue treatment
2 or more months	Yes (3 samples)	Negative or EPTB	-	Clinical decision on individual basis whether to restart or continue treatment, or no further treatment

		If 1 or more positive	-	Cat 1: Start Cat 2 and send sample for rapid DST
				Cat 2: Send sample for rapid DST and continue treatment

4.4 Managing transfer-in and transfer-out

When a patient transfers out to another treatment facility, it should be indicated in the Regional/ Central TB register. The date of transfer-out and the new treatment facility must be indicated. Transfer-out forms must accompany the patient and must be sent to the new treatment facility.

A copy of each transfer-out form must be sent to the LTI of the receiving facility. A copy of each transfer-out form must be kept at the original treatment unit in a special transfer-out folder.

When patients transfer in from another facility, they should be registered in the transfer-in register. The patient's treatment outcome must be entered in the transfer-in register; and results must be communicated to the original treatment unit. Transfer- in registers must be properly filled in. Just like the main register, TB officers must indicate when quarters start and finish. All transfer-in forms must be kept in a special transfer-in folder.

4.5 Recording outcome of treatment

It is vital for assessing programme performance that accurate recording of treatment outcome results are entered in the TB registers and treatment cards for ALL patients. Treatment cards for patients who have completed treatment, died or defaulted must be collected from health centres. These treatment cards must be kept safely and in chronological order in the TB office.

At the end of treatment, results of chemotherapy should be recorded according to treatment outcome

Table 4.11: Definitions of treatment outcomes

Cured	A patient whose sputum smear or culture was positive at the beginning of treatment but is smear- or culture- negative in the last month of treatment and on at least one prior occasion.
Treatment completed	A patient who has completed treatment (with a full course of TB treatment) but does not have a negative smear or culture result from the last month of treatment and at least one prior occasion.
Treatment Failure	A patient whose sputum smears or culture is positive at 5 months or later during treatment (Of note, also included in this definition are patients found to have MDR-TB at any point during treatment, regardless of whether they

	were initially smear-negative or -positive.) [b]
Died	A patient who dies for any reason during the course of their treatment.
Defaulted	A patient whose treatment was interrupted for two consecutive months or more.
Transferred out	Patient who has been transferred to another treatment centre and in whom the treatment outcome is not known.
Treatment success	A sum of cured and completed treatment

[a] These definitions apply to pulmonary smear-positive and smear-negative patients, and to patients with extra-pulmonary disease. Outcomes in these patients need to be evaluated separately.

[b] The sputum examination may not have been done or the results may not be available.

[c] For smear- or culture-positive patients only.

Within the NLTP, the outcome of treatment of all TB cases is evaluated quarterly using Tuberculosis cohort report forms

4.6 Management of contacts

A contact investigation is the process of identifying, examining, evaluate all persons who are at risk for infection with *Mycobacterium tuberculosis* due to recent exposure to a newly diagnosed or suspected case of pulmonary, laryngeal, or pleural tuberculosis (TB).

The primary goal of a contact investigation is to

- Identify persons who were exposed to an infectious case of TB
- **Ensure that contacts receive**:
- Testing for *M. tuberculosis* infection;
- Screening for TB disease;
- Medical evaluation, if indicated;
- Prompt initiation of treatment for latent tuberculosis infection (LTBI) if at high risk (younger than 5 years of age or immune-compromised); and
- Complete, standard course of treatment, unless medically contraindicated.[i]

Contacts of all smear positive PTB patients should be invited and screened for tuberculosis. These include:

- All adult contacts that are coughing for 2 weeks or more.
- Those with known positive HIV Status (with or without cough). They have higher risk of progression to disease
- All children of under 5 in the household including those born while on treatment.

Health worker should keep a record of all contact persons examined.

- Contacts who have symptoms of Tuberculosis should be fully evaluated.
- If tuberculosis disease is confirmed, patient should receive full treatment of Tuberculosis.
- If patient has a known HIV status, and has no symptoms of tuberculosis, a course of isoniazid preventive therapy is administered. See Chapter 7.3.3 for details.
- For child contact with no symptom of Tuberculosis, isoniazid preventive therapy must be administered. See Chapter 6.10 and 6.14 for instructions on Isoniazid Preventive therapy for children

5.0 Management of complications

5.1 The management of common TB-related complications

The management of common TB-related complications are outlined in Table 5.1.

Table 5.1: TB-related complications

Complication	Management
Haemoptysis (coughing up blood)	Admit patient to hospital for oxygen, blood transfusion and intubation if bleeding is severe
	Put the patient on the lateral position.
	Request chest x-ray to rule out conditions such as invasive aspergillosis or bronchiectasis.
Pleural effusion or empyema	This may subside with TB treatment alone but sometimes drainage is necessary to relieve symptoms of dyspnoea.
	All empyema should be drained
Spontaneous pneumothorax	Admit patient to hospital for placement of a chest tube and drainage with an underwater seal.
Paraplegia (may be due to spinal TB)	Refer the patient to the hospital. Surgery may be needed
TB meningitis	High doses of steroids
Cold abscesses and suppurating fistulae	Drainage of abscesses

Complication	Management
TB pericarditis	High doses of steroids (see Table 6.7)
	Cardiac tamponade (i.e. distress associated with shock) may necessitate pericardial aspiration by an experienced clinician.

5.2 Adverse (side) effects of anti-TB drugs

Most TB patients complete their treatment without any significant adverse drug effects. However, a few patients do experience adverse effects. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly Health personnel can monitor adverse drug effects by teaching patients how to recognize the symptoms of common effects, urging them to report if they develop such symptoms, and by asking about symptoms when patients come to collect drugs.

Some side effects can be hazardous for the patient's health or may force the patient to stop treatment. In general, a patient who develops a minor adverse side effect should continue the TB treatment and be given symptomatic treatment. If a patient develops a severe side effect, the responsible drug (or the entire regimen if the culprit drug cannot be identified) should be stopped and the patient should be referred. Common side effects are listed in Table 5.2.

Adverse reactions to drugs should be recorded on the TB Treatment Card. A reporting form for adverse drug reaction (ADR) must also be completed and sent according to guidelines.

Table 5.2: Symptom-based approach to managing major side effects of anti-TB drugs

Major side effects: Stop responsible drug(s) and refer to clinician urgently

Side effects	Drug(s) probably responsible	Management
Skin rash with or without itching	S, H, R, Z	Stop anti-TB drugs and refer to hospital
Deafness (no wax on otoscopy)	S	Stop streptomycin and refer to hospital
Dizziness (vertigo and nystagmus)	S	Stop streptomycin and refer to hospital
Jaundice (other causes excluded), hepatitis	H, Z, R	Stop anti-TB drugs and refer to hospital
Visual impairment (other causes	E	Stop ethambutol and refer to

Side effects	Drug(s) probably responsible	Management
excluded)		hospital
Shock, purpura, acute renal failure	R	Stop rifampicin and refer to hospital

Table 5.3: Symptom-based approach to managing minor side effects of anti-TB drugs

Minor side effects: Continue anti-TB drugs, check doses

Side effects	Drug(s) probably responsible	Management
Anorexia, nausea, abdominal pain	Z, R, H	Give drugs with small meals or just before bedtime;
		Advise patient to swallow pills slowly with small sips of water; If symptoms persist or worsen, refer to hospital
Joint pains	Z	Non-steroidal anti- inflammatory (e.g. brufen) or paracetamol
Burning/numbness in the hands/ feet	H	Pyridoxine 50 -75mg daily
Orange/red urine	R	Reassure, counsel patients before starting treatment
Drowsiness	H	Reassurance. Give drugs before bedtime
Flu syndrome (fever, chills, malaise, headaches, bone pains)	Intermittent dosing of Rifampicin	Change intermittent to daily rifampicin administration

5.3 Cutaneous and generalised hypersensitivity reaction skin eruptions

If a patient develops itching without a rash and there is no other obvious cause, the recommended approach is to try symptomatic treatment with antihistamines and skin moisturizing, and continue TB treatment while observing the patient closely. If a skin rash develops, however, all anti-TB drugs must be stopped. If the rash is severe, or there is

evidence of mucosal involvement or hypotension, corticosteroid treatment (1 mg/kg prednisolone) should be instituted. The amount of prednisolone is gradually reduced in the following days according to the patient's response. In patients with severe reactions, anti-TB treatment sometimes has to be stopped for 3-4 weeks. Do a liver function test.

Re-introduction of anti-TB drugs

Once the reaction has resolved, anti-TB drugs are reintroduced one by one, starting with the drug least likely to be responsible for the reaction (rifampicin or isoniazid) at a small challenge dose, such as 50 mg isoniazid. The dose is gradually increased over 3 days. The procedure is to observe if the patient tolerates a full dose of isoniazid before adding rifampicin, then evaluate if the patient tolerates a full dose of rifampicin before introducing pyrazinamide, and so on. A reaction after adding in a particular drug identifies that drug as the one responsible for the reaction. Refer to Table 5.4 below for further guidance on reintroduction of anti-TB drugs.

Table 5.4: Challenge doses

Drug	Day	Dose 1	Dose 2	Dose 3
Isoniazid (H)	1	50mg		
	2		300mg	
	3			300mg
Rifampicin (R)	4	75 mg		
	5		300 mg	
	6			Full dose
Pyrazinamide (Z)	7	200 mg		
	8		800 mg	
	9			Full dose
Ethambutol (E)	10	100 mg		
	11		400 mg	
	12			Full dose
Streptomycin (S)	13	125mg		
	14		500mg	
	15			Full dose

The drugs at the top of the table are the least likely to cause a reaction, and should be reintroduced first. Those at the bottom of the table are most likely to cause a reaction. If the initial cutaneous reaction was severe, smaller initial challenge doses should be given, approximately 1/10 of the doses shown for Day 1. If a patient is recommenced on an adequate anti-tuberculosis treatment regimen (e.g. isoniazid, rifampicin and pyrazinamide), then re-challenging with the implicated drug (e.g. streptomycin) is not advisable.

5.4. Drug-induced hepatitis

Mild, symptomless increases in serum liver transaminases occur during the early weeks of treatment. There is no need to interrupt or change treatment unless there is anorexia, malaise or vomiting or clinically evident jaundice with hepatic enlargement. Clinical features of concern include protracted vomiting, jaundice, mental status changes and signs of bleeding—all these suggest impending acute liver failure.

If jaundice or any of the clinical features suggestive of acute liver failure develops, all drugs must be stopped until the jaundice or hepatic symptoms have resolved and the liver function tests have reverted to normal. If liver function tests cannot be measured, then it is advisable to wait an extra two weeks after the jaundice has disappeared before recommencing anti-TB therapy.

Once the drug-induced hepatitis has resolved, the drug regimen can be re-introduced, although it is safer to avoid pyrazinamide. Therefore, in the initial phase, a regimen of isoniazid, rifampicin and ethambutol could be used, followed by rifampicin and isoniazid in the continuation phase. If there has been severe hepatitis; however, it is probably safer to use the previous standard regimen of streptomycin, isoniazid and ethambutol.

Severely ill patients with TB who develop drug-induced hepatitis should have the drug regimen stopped. If it is felt that anti-TB treatment should continue, then interim therapy may be started with streptomycin and ethambutol.

5.5 Pharmacovigilance

5.5.1 What is Pharmacovigilance

Pharmacovigilance is the Science and activities relating to the detection, assessment, understanding, response and prevention of adverse drug reactions (ADRS) and other potential medicine-related problems.

5.5.2 Aims of Pharmacovigilance

a. Improve patient care and safety
b. Improve public health and safety for all medicines
c. Assess benefit, harm, effectiveness and risk of medicines
d. Encourage safe, rational and cost effective use of Medicines
e. Effectively communicate Surveillance results to the Public
f. Promote understanding, education and clinical training in Pharmacovigilance

5.5.3 What to do when Adverse Drug Reactions are suspected during TB treatment

a. Interview and examine the patients
b. Document your findings in the patient treatment card

c. Take appropriate action as outlined in tables 5.2 and 5.3 above. Some patients might have to be transfer to the hospital.
d. Compete the Adverse Drug Reaction (ADR) form for the patient.
e. Duly completed form must be submitted to office of the Regional Public Health nurse who is the pharmacovigilance focal point at the regional level.

6 Childhood Tuberculosis

6.1 Investigation and management of children suspected to have TB or who are close contacts of a TB case (sputum smear-positive or -negative)

The recommended approach to diagnosing TB in children includes (see Figure 6.1):

- Gathering a detailed patient history, including history of TB contacts and symptoms consistent with TB;
- Clinical examination including growth assessment;
- HIV testing: provider initiated testing and counselling (PITC);
- Sputum microscopy and culture when possible (especially in children > 8 years of age); and
- Mantoux test (tuberculin skin test) if available.

The presence of any of the following strongly suggests a diagnosis of TB:

- Current cough of any duration (productive or non- productive in nature)
- Unexplained weight loss
- Failure to thrive and/or malnutrition
- History of contact with a TB case
- Fever and/or night sweats

All children with symptoms suggestive of TB should be investigated. Children can present with TB at any age but it is most common in the under-5 age group and during adolescence. The following symptoms are suggestive of TB meningitis, especially in young children with TB exposure:

- Decreased appetite, often with weight loss;
- Vomiting without diarrhoea, early morning headache, irritability;
- Drowsiness/lethargy and convulsions, especially focal seizures;
- Behavioral changes (irritability, confusion or agitation).

- Children who are close contacts of an infectious TB case are at high risk of becoming infected with M. tuberculosis and developing active TB.
- Clinicians should have a low threshold for investigating TB and commencing young children on TB treatment.
- Once an adult contact is confirmed, the main clinical decision is whether the child needs full 4-drug treatment or isoniazid preventive therapy (IPT) chemoprophylaxis.

6.2 Physical findings suggestive of TB in children

Physical findings suggestive of TB in children include:

- Abnormalities detected when listening to the lungs: crackles, coarse breath sounds, etc.;
- Dullness to percussion of the chest may suggest a TB pleural effusion;
- A painless, enlarged mass of lymph nodes in the neck, without response to a course of antibiotics, is highly suggestive of TB cervical adenitis; and
- Other features of EPTB (see Table 6.1) below for summary of diagnostic approach to EPTB.

6.3 Laboratory diagnosis of PTB in children

6.3.1 SPUTUM COLLECTION

TB in children is usually sputum smear-negative. Collection of sputum specimens is difficult since children usually swallow their sputum. Sputum in younger children with TB contains few TB bacilli, but this is not true for older children (> 8 years of age). The sputum smear (and sputum for Xpert MTB/RIF or TB culture, where available) remains a valuable test to perform in any child who is able to produce a sputum specimen.

In children who are unable to expectorate spontaneously, obtaining an aspirate of gastric fluid is a reasonable alternative to obtaining sputum. Gastric aspirates are safe and easy to perform in hospital after a 3-hour fast or early in the morning after an overnight fast.

6.3.2 FINE NEEDLE ASPIRATION (FNA)

In children with large, palpable cervical lymph nodes, collection of an aspirate offers a convenient way of collecting samples for microscopy and culture. The aspirate can be smeared onto a slide and sent for microscopy where culture is not available.

6.3.3 LUMBAR PUNCTURE (LP)

Should be performed on any child in whom TBM is suspected and repeated on a child failing to respond to standard treatment for bacterial meningitis. Suspect TBM if the CSF demonstrates an elevated WBC count with a lymphocytic predominance, a high protein level and/or a low glucose concentration. Absence of bacilli on microscopy does not exclude a diagnosis of TBM. TB culture is of particular value when there is a concern regarding drug resistance. The probability of obtaining a positive TB culture result increases when more than one sample is taken.

6.3.4 Chest x-ray

Chest X-ray remains an important tool for diagnosis of PTB in children who are sputum smear negative or who cannot produce sputum. Chest x-rays need to be of good quality and interpretation depends on the expertise of the person reading them.

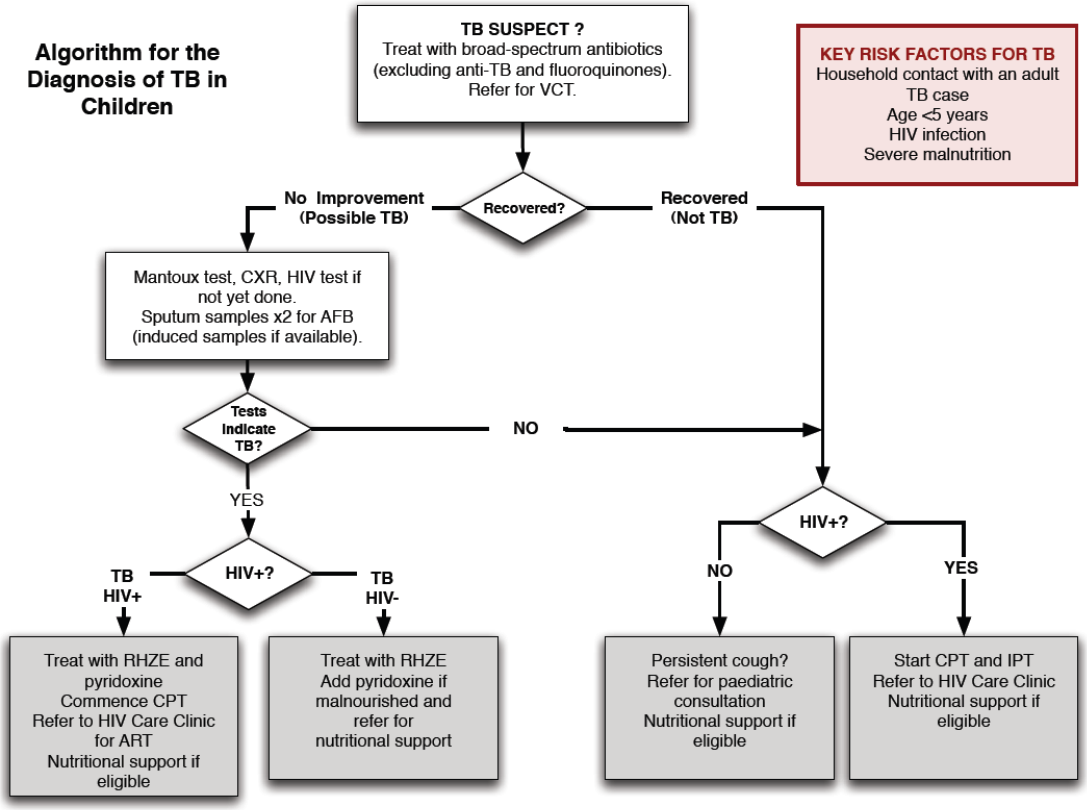
CXR changes are often non-specific and may be completely normal in the HIV-infected or malnourished child. TB disease should not be diagnosed from the CXR alone. The whole clinical picture should be taken into account.

The following abnormalities on Chest X-ray are suggestive of TB:

- Enlarged hilar lymph nodes and opacification in the lung tissue
- Widened mediastinum due to enlarged lymph nodes (this is the most common x-ray abnormality in children with TB).
- Following dissemination, miliary disease may present as scattered markings across the lungs fields on x-ray
- Cavitation (tends to occur in older children)
- Pleural or pericardial effusion – though seen on CXR – are forms of extra pulmonary TB that tend to occur in older children (> 5 years of age)

The finding of marked abnormality on CXR in a child with no signs of respiratory distress (no fast breathing or chest in-drawing) is supportive of TB

Figure 6.1: Diagnostic pathway in children



6.3.5 Tuberculin Skin Test (TST)— Mantoux Test

The Mantoux test measures the delayed-type hypersensitivity response to purified protein derivative (PPD) a protein precipitate of inactivated tubercle bacilli. PPD is also known as tuberculin. A positive Mantoux does not indicate active TB disease; it only indicates latent infection with M. tuberculosis (LTBI). The Mantoux test is positive when the diameter of skin induration (swelling, not redness) is ≥ 10 mm (or ≥ 5 mm in an HIV-infected or malnourished child). A negative TST does not exclude TB infection or disease.

The tuberculin skin test may be *falsely negative* in a child with:

- Severe malnutrition
- HIV infection
- Disseminated (miliary) TB and/or TB meningitis •
- Very young children (≤ 12 months)

6.3.6 HIV test

- *Any child with suspected TB should have an HIV test*
- A positive HIV test also directs the need for other HIV-related care for the child and possibly other family members

6.4 Clinical Diagnosis of Extra-Pulmonary Tuberculosis

6.4.1 Clinical features and suggested investigations for each category

Extra-pulmonary TB is common in children and presentation varies with age. The table below lists typical clinical features of forms of EPTB and suggested investigations for each category. Symptoms vary depending on site of disease and characteristically are persistent, progressive and may be associated with weight loss or poor weight gain

Clinical assessment in all cases should consider:

- **History of contact** Time lapse from exposure to disease presentation can be quite variable – shorter for young children with disseminated disease, longer for other forms that present in school-aged children
- **Sputum for smear microscopy** if cough and sputum is available
- **HIV test**

Table 6.1 Summary of diagnostic approach to EPTB

Site of EPTB	Typical clinical presentation	Investigation	Comment
TB adenitis	Asymmetrical, painless, non-tender lymph node enlargement for more than one month +/- discharging sinus Most commonly in neck area	Fine needle aspiration when possible for culture and histology TST usually positive - not necessary for diagnosis	Treat If axillary node enlargement on same side as BCG, consider BCG disease and refer
Pleural TB	Dullness on percussion and reduced breath sounds +/-chest pain	CXR Pleural tap#	Treat If pus in pleural tap, consider empyema and refer
Usually young (< 5 years) with disseminated disease and severely ill			
TB meningitis	Headache, irritability/abnormal behaviour, vomiting (without diarrhoea), lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle, cranial nerve palsies	Lumbar puncture obtain CSF# CXR	Hospitalise for TB treatment §
Miliary TB	Non-specific, lethargic, fever, wasted	CXR	Treat and refer §
Usually 5 years and older			
Abdominal TB	Abdominal swelling with ascites or abdominal masses	Ascitic tap#	Refer §
Spinal TB	Deformity of spine May have lower limb weakness/paralysis/unable to walk	X-ray spine	Refer §
Pericardial TB	Cardiac failure Distant heart sounds Apex beat difficult to palpate	CXR Cardiac ultrasound Pericardial tap#	Refer §
TB bone and joint	Swelling end of long bones with limitation of movement Unilateral effusion of usually knee or hip	X-ray bone/joint Joint tap#	Refer §

Typical findings: straw colored fluid, exudate with high protein, white blood cells predominantly lymphocytes on microscopy

Referral may be necessary for investigation procedure and laboratory support as well as clinical care. If all options for referral have been explored and referral is not possible, start anti-TB treatment. Start anti-TB treatment immediately if TBM suspected

6.4.2 TB adenitis

Tuberculous lymphadenitis is the commonest form of EPTB in children, usually representing around 10% of total child TB caseload. Enlargement of regional lymph nodes occurs after infection via lymphatic drainage from the site of infection. TB adenitis may or may not be associated with other symptoms of TB. Sinus and discharge may develop.

The cervical lymph nodes are the commonest site of clinical presentation. The usual age of presentation is 2-10 years.

Lymph node enlargement due to TB is typically:

- Large (>2 x 2 cm) i.e. visibly enlarged not just palpable.
- Painless and asymmetrical - often multiple, discreet or matted
- Persistent (>1 month) and not responsive to other treatment such as antibiotics

Result of TST (if available) is usually strongly reactive but this is not necessary for diagnosis. Fine needle aspiration for culture and histology should be done whenever possible.

6.5 Treatment of paediatric TB: first-line TB regimen

Table 6.2: Revised treatment guidelines for paediatric TB

Date or type of TB disease	RHZE Treatment duration	RH Treatment duration	Total length of treatment
TB meningitis Miliary TB Osteoarticular TB (spine, joints)	2 months	10 months	12 months
Pulmonary TB TB lymphadenitis ALL other forms of TB	2 months	4 months	6 months

H=isoniazid. R=rifampicin. Z=pyrazinamide. E=ethambutol
Numeral refers to number of months of the regimen e.g. 2 HRZE refers to two months of daily isoniazid, rifampicin, pyrazinamide and ethambutol

Note:

- Streptomycin no longer recommended for new patients
- Intermittent regimens not recommended in HIV-endemic setting

Table 6.3: TB paediatric drug dosages

Drug	Dosage
Isoniazid (H)	10 mg/kg (range 10 – 15 mg/kg); max. dose 300 mg/day
Rifampicin (R)	15 mg/kg (range 10 – 20 mg/kg); max. dose 600 mg/day
Pyrazinamide (Z)	35 mg/kg (range 30 – 40 mg/kg); max. dose 2000 mg/day
Ethambutol (E)	20 mg/kg (range 15 – 25 mg/kg) max; 1200 mg/day

It is important to monitor the child's weight at every clinic visit and to adjust drug doses accordingly. Many children rapidly gain weight after initiation of TB treatment.

- Nutritional support should be provided for malnourished children if available
- Breastfeeding infants and children should continue to breastfeed while receiving anti-TB treatment
- Pyridoxine is not routinely given but is recommended for severely malnourished and HIV-infected children

Table 6.4: Drug regimen and dosages for New PTB cases **(2RHZ+E/4RH): Children**

Weight Bands	**Number of Tablets**		
	Intensive Phase (2 months)		**Continuation Phase (4 months)**
	RHZ (60mg+30mg+150mg)	**E (100mg)**	**RH (60mg + 60mg)**
4 – 6 kg	1	1	1
7 – 10 kg	2	2	2
11 – 14 kg	3	2	3
15 – 19 kg	4	3	4
20 -24 kg	5	4	5
25 – 29 kg	**Refer to drug and regimen table for adults**		

Table 6.4: Drug regimen and dosages for TB Meningitis and osteo articular TB **(2RHZ+E/10RH): Children**

Weight Bands	**Number of Tablets**		
	Intensive Phase (2 months)		**Continuation Phase (10 months)**
	RHZ (60mg+30mg+150mg)	**E (100mg)**	**RH (60mg + 60mg)**
4 – 6 kg	1	1	1
7 – 10 kg	2	2	2
11 – 14 kg	3	2	3
15 – 19 kg	4	3	4
20 -24 kg	5	4	5
25 – 29 kg	**Refer to drug and regimen table for adults**		

Table 6.5: Drug regimen and dosages for previously treated TB cases 2(RHZE)S/1(RHZE)/5(HRE).

Weight Bands	**Number of Tablets**				
	Intensive Phase (3 months)			**Continuation Phase (5 months)**	
	RHZ (60mg+30mg+150mg)	**E (100mg)**	**S (only in the first 2 months of intensive phase**	**RH (60mg + 60mg)**	**E (100mg)**
4 – 6 kg	1	1	0.25 gm.	1	1
7 – 10 kg	2	2	0.25 gm.	2	2
11 – 14 kg	3	2	0.25 gm.	3	2
15 – 19 kg	4	3	0.50 gm.	4	3
20 -24 kg	5	4	0.50 gm.	5	4
25 – 29 kg	**Refer to drug and regimen table for adults**				

6.6 Use of adjuvant therapy in TB treatment

Use of steroids

In TB meningitis and pericardial effusion, steroids have a supportive therapeutic effect. Steroids have been shown to improve survival in patients with TB meningitis and decrease the risk of developing constrictive pericarditis in patients with pericardial effusions.

Prednisolone dosage (first-line): 2 - 4 mg/kg/day (maximum dose of 40 mg) for three weeks, followed by a reduction regimen over three weeks.

Use of Pyridoxine (Vitamin B6)

Pyridoxine (vitamin B6) protects against isoniazid-induced peripheral neuropathy. Pyridoxine is recommended for all children on TB treatment and IPT. The recommended dose is 25 mg/ day until treatment is completed.

6.7 Treatment Monitoring

Treatment of HIV-uninfected: is monitored monthly during intensive phase and 2-monthly on continuation phase

For HIV-infected: review at 2 weeks and 4 weeks following commencement of anti-TB treatment and then monthly thereafter

Important practice points

- Weigh the child at each follow-up, document and adjust dosage if necessary
- Adherence for the full course of treatment may be a challenge.
    - Explain and emphasize to care-giver and child why they must take the full course of treatment even if they are feeling better
    - Note risk factors for poor adherence such as distance/transport; orphan (especially if mother has died) or primary care-giver unwell; adolescents
    - Education and adherence support especially TB/HIV
- Explain that anti-TB drugs in children are well tolerated and safe.
- Chest X-ray is not required in follow-up if the child is responding well to anti-TB treatment

The most important adverse effect is hepatitis which usually presents with jaundice, nausea and vomiting. There may be abdominal pain, jaundice and tender, enlarged liver.

If considered a possibility, stop the anti-TB drugs immediately and refer to hospital

6.8 Treatment failure

Most children with TB will start to show signs of improvement after 2 to 4 weeks of anti-TB treatment

Assessment at 1-2 months after treatment, consider treatment failure if child is receiving anti-TB treatment and:

- No symptom resolution or symptoms getting worse
- Continued weight loss
- Smear-positive at 2 month follow-up sputum

Poor adherence is a common cause of “treatment failure”.

If a child stops anti-TB treatment for more than 2 weeks in the intensive phase or more than 2 months in the continuation phase and becomes symptomatic, then restart first-line anti-TB therapy. If a child stops anti-TB treatment for less than 2 weeks in the intensive phase or less than 2 months in the continuation phase and becomes symptomatic, then continue current regimen.

Treatment failure is more common in HIV-infected children.

Treatment failure suggests the possibility of MDR TB and needs careful assessment.

Refer children with treatment failure for further assessment

6.9 Paediatric multidrug-resistant TB

Children with proven or suspected TB caused by multidrug- resistant bacilli should be treated with an appropriate MDR-TB regimen.

Suspect MDR-TB in any child:

- Who is a contact of an adult MDR-TB case and has symptoms and signs suggestive of TB disease.
- Who remains symptomatic after completion of first-line TB treatment with good medication and adherence.

6.10 Prevention of TB in Children

Irrespective of age, all children who are household contacts of infectious TB cases should be evaluated for TB disease and either treated for TB or given preventive therapy if screening finds that they are unlikely to active TB

6.10.1 BCG vaccine and BCG Disease

Bacille Calmette-Guerin (BCG) is a live, attenuated vaccine and is routinely given to neonates in The Gambia in the first week of life. BCG may be associated with injection-site abscesses, adenitis, and (very rarely) with disseminated disease. Infants with advanced HIV infection are at particular risk of BCG-related complications. The presence of right-sided axillary or regional lymph nodes in a young child or infant indicates possible BCG disease and an immune-compromised state. This most commonly presents in the two years of life after BCG vaccination. It requires further evaluation. Refer to experienced clinicians if BCG disease is suspected

6.10.2 Contact management and Isoniazid preventive therapy (IPT)

A contact is a person who has a history of a close contact with an adult patient with pulmonary TB (sputum smear-positive or smear-negative). Contacts are eligible for IPT. However active TB should be ruled out before starting IPT. For any child with contact history, 6 months of IPT is indicated, even if he or she is on ART. For HIV-infected children

not on ART, IPT is to be given for the entire time period until ART is initiated, regardless of contact history. A CXR is recommended, but not required, to rule out active TB in HIV-infected and -exposed children with a positive contact history.

If children have NONE of the following signs or symptoms, then active TB can be ruled-out without TST or CXR:

- Poor weight gain
- Chronic cough
- Fever

For all paediatric age groups, the recommended dosing of IPT is 10 mg/kg once daily for 6 months.

Patients should not be given a 6-month supply to take home. Patients should be monitored every two months at a minimum to check for medication toxicity or development of active TB. Children < 1 year of age should be weighed monthly and the dose of isoniazid adjusted for changes in weight. If a child develops signs and symptoms of active TB while on IPT, then isoniazid should be stopped and the patient should be re-assessed and started on full TB treatment. All HIV-infected children must receive pyridoxine (25 mg/day) for the duration of IPT.

6.10.3 Neonate exposed to a mother with TB

If a mother is diagnosed with TB before the third trimester of pregnancy, is taking TB medications with good adherence and is clinically well:

- Examine the newborn for signs of disease. If the baby is well, no action is required.
- Refer all other household children <5 years of age to the TB clinic for clinical assessment.

If a mother is diagnosed with TB in the third trimester of pregnancy or shortly after delivery, examine her baby closely for symptoms and signs of disease. If the baby is well, commence isoniazid (H) prophylaxis at 10 mg/kg/day and continue for 6 months.

Do not give BCG vaccine. If the baby is not well and has signs/symptoms suggestive of TB disease, collect gastric aspirates where possible for investigation and/or commence full TB treatment.

Infants need to be reviewed at 1, 3 and 6 months after commencing isoniazid. Infants' weights must be checked regularly and their isoniazid dosages increased as they grow.

Refer all other household children to the TB clinic for clinical assessment and screening. As BCG is a live vaccine, isoniazid will kill the vaccine and prevent an effective immune response from developing. If isoniazid is commenced within 12 weeks of receiving BCG vaccination, the infant will need repeat BCG vaccination following the end of treatment. If

no BCG vaccine was given at birth, then vaccinate the baby two weeks after completing isoniazid.

- IPT is intended to prevent recent TB infection from progressing to active TB disease and to prevent latent TB infection (LTBI) from reactivating.
- IPT is given for six months after a TB contact.
- If a patient is diagnosed with active TB they need full TB treatment and not isoniazid monotherapy.

6.11 TB and HIV infection in children

The current approach to clinical diagnosis of TB in HIV-infected children is similar to that recommended for HIV-uninfected children (see Figure 6.1). It is recommended that HIV-infected children be treated with the same TB treatment regimens and for the same duration as those for HIV-uninfected children. Children with TB/HIV must be followed up with regularly and have dosages adjusted for changes in weight. HIV-infected children being treated for TB must be started on co-trimoxazole preventive therapy (CPT).

HIV-infected children should also be started on ART as soon as the TB treatment is commenced. ART can be started on the same day as TB treatment if the child is stable.

6.11.1 Antiretroviral therapy in Children with TB/HIV Co-Infection

ART is indicated for all HIV-infected children and infants with any form of TB. Children must be followed up regularly. Patients must be weighed at regular intervals and adjust dosages for both anti-TB and ART. Refer those children who are co-infected to the ART clinic for HIV treatment and care.

6.11.2 Co-trimoxazole preventive therapy

Daily CPT prophylaxis prolongs survival in HIV-infected children and reduces the incidence of co-morbidities. It also reduces the risk of co-infections such as PcP in HIV-exposed infants. Therefore, CPT is recommended for all HIV-exposed infants and HIV-infected children, including those with TB. Dosages are listed by weight or age in Table 6.6.

Table 6.6. Recommended doses of daily CPT by age or weight

Recommended daily dosage based on age or weight (see legend)		Suspension (5 ml syrup of 200mg/40mg)	Child tablet (100mg/20mg)	Single strength adult tablet (400mg/80mg)
< 6 months	< 5 Kg	0.5 ml	One tablet	¼ tablet
6 months to 5 years	5-15 Kg	5 ml	Two tablets	Half tablet
6 – 14 years	15-30 Kg	10 ml	Four tablets	One tablet

7 Managing Tuberculosis and HIV Co-infection

7.1 The Interaction Between TB And HIV

Infection with HIV leads to destruction of the body's immune system. Persons who are infected with HIV are therefore more prone to TB disease than those without HIV infection. A strong immune system usually prevents the development of TB disease following infection with TB bacilli. HIV reduces the protection provided by the immune system and enables TB bacilli to multiply unchecked, facilitating rapid progression to active TB disease. HIV-related tuberculosis is associated with poor TB treatment outcomes. It is therefore imperative to rapidly identify and treat TB cases among PLHIV effectively.

7.2 Impact of HIV on TB

High HIV prevalence is associated with an increase in the number of new TB cases. HIV infection increases susceptibility to new TB infections and accelerates the progression from LTBI to active TB disease. In particular, HIV is associated with an increase in smear-negative and EPTB cases.

Smear-negative TB and EPTB are more common in HIV-infected TB patients. Most HIV patients with TB do not have typical TB symptoms (productive, chronic cough etc.). In Gambia about 24% of all TB cases are smear-negative and 7% (NLTP notification data 2010) are EPTB. When HIV-positive patients develop PTB, the number of bacilli secreted into the sputum is fewer than in HIV-negative patients. This makes diagnosis by conventional microscopy difficult. Studies show that up to 17% of new TB cases are acquired from smear-negative cases. It is important to identify and treat smear-negative cases early in order to break the cycle of TB transmission in the community and health facilities.

HIV infection increases TB-associated morbidity and mortality. HIV-positive TB patients have a higher case-fatality during TB treatment compared with HIV-negative patients. HIV-positive, smear-negative patients and EPTB patients have worse treatment outcomes than in smear-positive TB patients. Adverse reactions to anti-TB drugs are also more frequent in PLHIV compared to the general population, leading to interruptions of treatment and poor outcomes.

TB recurrence rates are higher in HIV-positive patients than in HIV-negative patients. Recurrence of TB may be from reactivation of persistent organisms not killed by previous anti-TB treatment or re-infection due to re-exposure to another infectious person.

MDR-TB has been reported amongst patients with HIV in the Africa Region. HIV does not itself cause MDR-TB, but it can increase the spread of this condition by increasing susceptibility to infection and accelerating the progression from infection to disease.

7.3 Collaboration and coordination between the TB and HIV programmes

7.3.1 Integrated TB/HIV Services

Controlling TB/HIV requires collaboration and coordination between the TB and HIV programmes at all levels. Service integration can include referral of patients and suspects between TB and HIV services, partial provision of joint TB/HIV services, or full integration of the TB and HIV/AIDS clinics. In order to minimize the burden to the patient it is advisable that the patient can receive both TB and ARV medicines from one health facility nearest to

his/her home or workplace. ARV drug collection should therefore be made accessible in health facilities that also offer TB therapy, or vice versa. When DOT is being given outside the health facility, ideally the ARV "treatment supporter" should also be the "DOT supporter", directly observing ingestion of both the ARV and TB medicines.

Examples of integrated TB/HIV services include:

- Provider-initiated HIV counselling and testing(PICT) of TB patients,
- Provision of co-trimoxazole preventive therapy (CPT),
- Early initiation of ART in HIV-infected patients with TB,
- Screening of all HIV-positive persons for active TB, and
- Provision of isoniazid preventive therapy (IPT) to PLHIV who do not have evidence of active TB.

7.3.2 Approach to diagnosis of TB in PLHIV

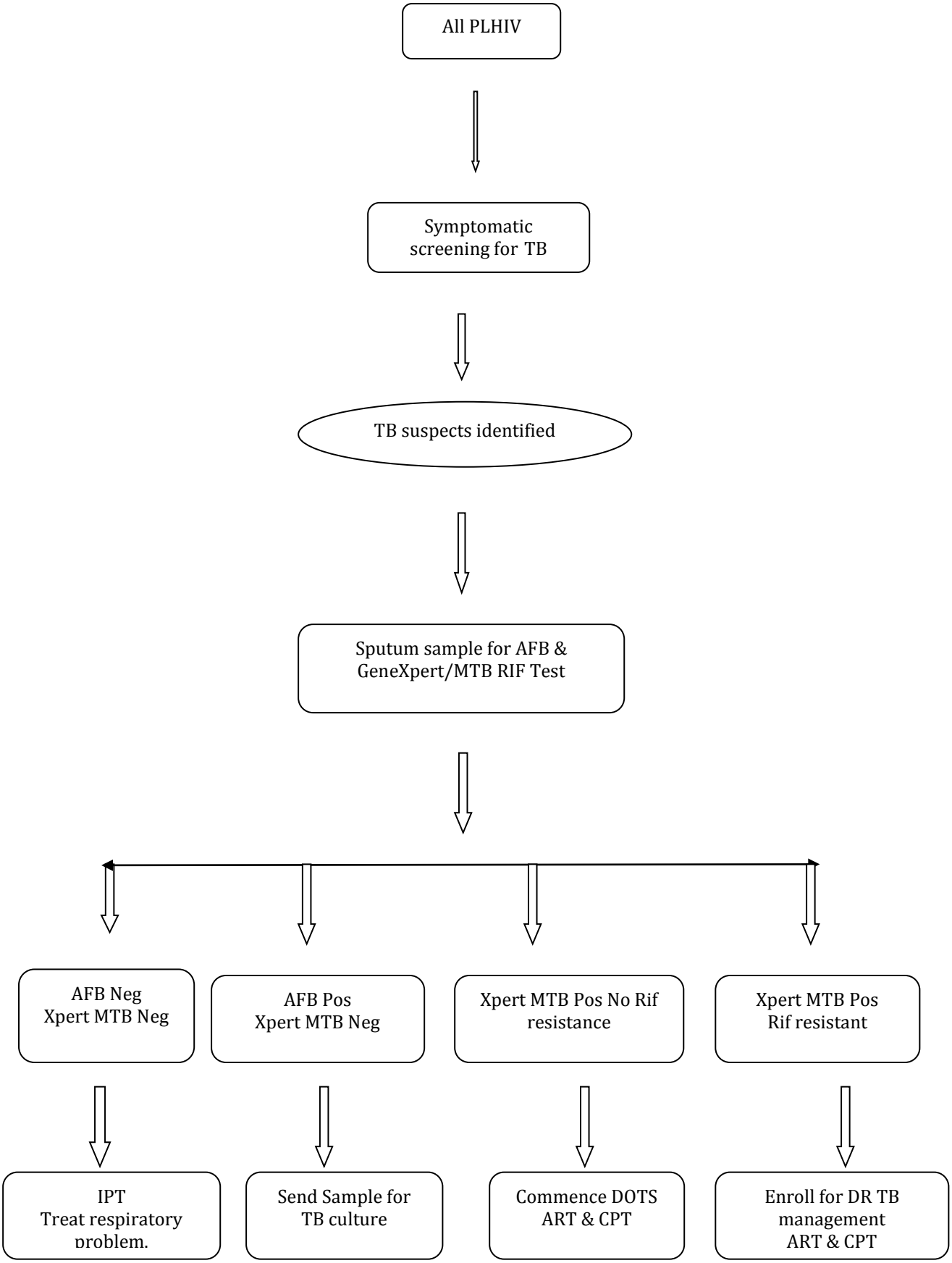
Early identification of TB cases and putting patients on effective treatment is important for TB control and reducing TB-related mortality, particularly in TB/HIV co-infected patients. Diagnosis of tuberculosis depends on the identification of the tubercle bacilli in sputum by microscopy, culture or newer molecular tests OR strong suspicion of TB based on sound clinical judgment. Refer to figure 7.1.

7.3.3 Provider-initiated HIV counselling and testing (PICT) for TB patients

All TB suspects and patients should be offered HIV counselling and testing by health workers. HIV testing should be carried out if HIV status is unknown, was previously reported as negative in the past 3 months or was refused or opted out of during the patient's previous visit. If a patient reports having been previously tested for HIV but has no documented evidence of this fact, the test should be repeated. All HIV-positive TB patients are entitled to quality HIV treatment, care and support services.

- It is important to note that HIV testing in TB patients and suspects is provider-initiated (PITC).
- Health workers should encourage HIV-positive TB patients to bring their partners and small children for HIV testing.

Figure 7.1 Algorithm for TB diagnosis among PLHIV



7.3.4 INH Preventive Therapy (IPT)

IPT has been shown to be beneficial in certain settings in preventing morbidity and mortality from TB. INH prophylaxis should be given to all HIV positive individuals in whom TB has been excluded.

IPT should also be given in the following circumstances:

- Children who are contacts of a smear positive TB case
- TB-exposed, HIV-infected children
- TB-exposed health care workers in whom active TB has been excluded

To exclude active TB:

- Ask the patient about cough, chest pain, fever, night sweats and weight loss etc
- Check for lymph node enlargement
- Those with the above symptoms/signs should not be considered for IPT
- Do sputum smear examination for AFB
- Refer/commence short course chemotherapy for TB (DOTS) if smear-positive
- Refer those with negative sputum smear results to medical officers for excluding active TB by chest X-ray or Xpert MTB/RIF or culture where available

Commence IPT, if no active TB is confirmed

Dosage of INH for adults is 300mg daily for 6 months. For children the daily dosage is 10mg/kg/body weight (maximum 300mg) for the same period.

7.3.5 Provision of co-trimoxazole preventive therapy

All HIV-positive TB patients should be started on CPT to reduce the occurrence of opportunistic infections. If possible, CPT should be started on the same day that the patient's HIV-positive status is determined.

The recommended dosage for trimethoprim-sulphamethoxazole (cotrimoxazole) 960mg daily .

Contraindications to cotrimoxazole include:

- Known severe drug reaction to sulphur-containing drugs,
- Severe megaloblastic anaemia or pancytopenia,
- End-stage renal disease.
- First trimester of pregnancy

Discontinuation of cotrimoxazole prophylaxis may be considered in those with evidence of good clinical response to ART

Refer to the national HIV treatment guidelines and NLTP SOP on CPT for further information.

7.3.6 Provision of antiretroviral therapy in HIV infected TB patients

Antiretroviral therapy improves survival in HIV-positive patients.

Regardless of CD4 count, all TB/HIV co-infected patients should be started on ART as soon as

possible and within the first 8 weeks of starting TB treatment. If the TB/HIV co-infected patient is clinically stable, ART and TB treatment may be started concurrently. The ART regimen for TB patients initiating antiretroviral therapy is a combination of Zidovudine/Lamivudine/Efavirenz [AZT/3TC/EFV) Refer to the National ART Treatment Manual 2011.

Initiation of ART is not an emergency, but untreated TB is highly fatal. Therefore TB treatment should be started first, followed by ART. All TB patients diagnosed with HIV should start CPT and follow referral protocol for ART as enunciated in the National ART Guidelines.

7.4 Immune reconstitution inflammatory syndrome (IRIS)

An HIV-positive patient's condition could worsen within the first 6 months of starting ART because of IRIS. IRIS is a result of recovery of the body's immune system. There are two common IRIS scenarios:

- An unmasking of an occult OI,
- A paradoxical symptomatic relapse or worsening of a prior infection that was seemingly diagnosed and treated successfully.

Before starting ART, counsel TB patients about the possibility of a temporary worsening of symptoms.

If a patient develops IRIS while on anti-TB treatment and ART, seek the advice of a senior ART provider or medical specialist. There is no need to stop or change TB or ARV treatment. Confirm that the patient adheres to his or her medication regimen as prescribed. Admit severe cases to hospital.

If treatment with steroids is indicated, give dexamethasone 8 – 16 mg/day (divided into twice daily dosing) or prednisolone 1 mg/kg body weight (once daily) for 14 – 21 days. After 14 – 21 days, rapidly taper the steroids over a 10 – 14 day period while monitoring for recurrence and/or worsening of symptoms.

Consider TB treatment failure or MDR-TB if the patient worsens despite having received one or more months of anti-TB treatment.

- Occasionally an HIV/TB co-infected patient may experience a temporary worsening of TB symptoms soon after beginning ART and TB treatment. IRIS should be considered as a potential cause of such clinical worsening.
- Signs and symptoms include: high fever, lymphadenopathy, and worsening CXR findings.
- Other causes of clinical worsening should be ruled out before making a diagnosis of IRIS; these include undiagnosed TB disease, cryptococcal meningitis and Kaposi Sarcoma.
- Patients with advanced AIDS who start ART late are at the greatest risk of developing IRIS.

7.5 Overlapping ARV and TB drug side effects

Concurrent use of ARVs and TB drugs has potential for added toxicity. The most common causes of skin rashes are pyrazinamide, isoniazid and rifampicin. ARVs such as nevirapine and efavirenz are also known to cause skin rashes. These overlapping side effects make it difficult to identify the causative drug when a patient is receiving treatment for both TB and HIV con- currently. Patients on both treatments need a thorough history and clinical assessment to establish which drug is responsible for the side effects.

Table 7.1: Drug interactions between ARVs and anti-TB drugs

Drug	Interactions with	What to do?
AZT	Cotrimoxazole, pyrimethamine	Check WBC and HB
3 TC	Cotrimoxazole: 3TC level increased	ll NIL (well tolerated
D4T	With drugs that cause neuropathy: INH, phenytoin, ethambutol	Use with caution or avoid
NVP	ketoconazole, rifampicin	Do not use
EFZ	carbamazepine, cisapride, ergot derivatives (ergotamine), ketoconazole Phenobarbital, phenytoin benzodiazepines Rifampicin Oral contraceptives	Do not use Only short term use possible Increase dosage to 800mg OD if tolerated Use dual protection
LPV/r	rifampicin, ergot derivatives, benzodiazepine, Phenobarbital phenytoin ketoconazole, itraconazole, carbamazepine, calcium channel blockers Oral contraceptives decreased effectiveness	Do not use Use with caution Dual protection essential
ABC	Alcohol	Avoid
DDI	Ethambutol Ketoconazole, doxycycline or ciprofloxacin (if buffered formulations)	Avoid Take 2 hours before or after meals

8 Multi-drug Resistant Tuberculosis

8.1 Definitions

In general, strains of TB can either be susceptible or resistant to anti-TB drugs:

- Susceptible TB refers to a tuberculosis strain that is not resistant to any anti-TB drugs.
- Drug-resistant TB is confirmed through laboratory tests that show that the infecting isolates of *M. tuberculosis* grow *in vitro* in the presence of one or more anti-TB drugs**.**

The types of different drug resistance are defined as follows:

- Mono- or poly-drug resistant TB: in this guideline we consider mono- or poly-drug resistant TB patients presenting with active TB due to an *MTB* strain that is resistant to at least H or R but not both at the same time.
- Multidrug-resistant TB (MDR-TB) is a form of tuberculosis in which the TB bacilli demonstrates resistance to, at a minimum, the two most powerful drugs used in first-line TB treatment, rifampicin and isoniazid.
- Extensively drug-resistant TB (XDR-TB) is MDR- TB plus resistance to any fluoroquinolone, and at least one of the three injectable second line anti-TB drugs (capreomycin, kanamycin or amikacin). Currently, The Gambia does not have the laboratory capacity to diagnose XDR-TB.

8.2 Extent of drug resistance in Gambia

The NLTP has set a target of providing access to DST for ALL previously treated TB patients before beginning retreatment. The purpose is to identify MDR-TB as early as possible so that appropriate treatment can be given. However, a national MDR-TB technical committee has been established comprising of MRC, NLTP, NPHL, WHO, NPS and other stakeholders chaired by the Director of Health Services. This committee meets on quarterly basis reviewing the culture and DST reports.

8.3 Causes of drug resistance

TB drug resistance is a man-made problem arising mainly from inadequate TB therapy caused by some of the factors listed in Table 8.1.

Table 8.1: Possible causes of drug resistance

Health care provider Inadequate regimen	Drugs Inadequate supply or poor quality	Patient Inadequate drug intake
• Inadequate guidelines	• Poor quality of drugs	• Poor adherence (poor DOT)
• Inappropriate guidelines	• Stock outs of certain drugs	• Lack of information
• Poor compliance with guidelines	• Poor storage conditions	• Lack of transportation
• Poor training	• Wrong dosage(s) or combination(s)	• Adverse or unpleasant side effects
• Absence of guidelines		• Social barriers
• No monitoring of treatment		

8.4 MDR-TB suspects/risk groups

An MDR-TB suspect is defined as a patient from one of the following risk groups:

- Patients who have had contact with a known MDR-TB patient;
- Contacts of a patient who died while on directly observed TB treatment;
- All patients, including retreatment cases, who remain smear-positive after 3 months of therapy with first-line drugs;
- All patients, including retreatment cases, who remain smear-positive after 5 months of therapy;
- New patients coming from areas with high prevalence of MDR-TB (certain parts of South Africa, Lesotho etc.);
- Patients previously successfully treated for TB;
- Health care workers in hospital/ health facility setting;
- Patients returning after default;
- Any patients in whom there is significant clinical concern for acquired resistance.

When encountering MDR-TB suspects, request the patient to submit sputum for microscopy, Xpert MTB/RIF, culture and DST. Manage patients according to results:

8.5 Testing for drug resistance

The initial screening test for DR-TB is the Xpert MTB/RIF. If the screening tests result is positive and with RIF resistance, culture and DST should be sent to confirm resistance. Treatment of MDR-TB should be started while waiting for confirmation. Sputum specimens should be submitted for Xpert MTB/RIF for all smear-positive and smear-negative MDR-TB

suspects as outlined in Section 8.4.

Culture and DST should be performed for any sputum sample found to be RIF resistance positive. Culture and DST can also be done when the sputum sample is RIF resistance negative but RIF resistance or other resistance is highly suspected clinically.

8.6 Collecting a sputum specimen for screening with Xpert MTB/RIF and for confirmation of resistance with culture and DST

The following outlines the roles and responsibilities for each member of the team.

Responsibilities of the clinician

- It is the responsibility of the clinician to arrange a screening test for MDR-TB with Xpert MTB/RIF under the indications described above and to follow up on the results with the patient. Screening tests requests with Xpert for DR-TB do not need to go through the LTI.
- For confirmation culture and DST, a sputum specimen requisition form must be completed by the ordering clinician and submitted to the LTI. The form asks for the patient's identifying and clinical information. A copy of the form will accompany the sample to the culture laboratory to link the sample to the patient and to provide a means of reporting the results of culture and DST back to the ordering clinician.

Responsibilities of the LTI

- The LTI should be aware of all Xpert MTB positive/RIF positive specimens and assure that a confirmation culture and DST is sent.
- For culture and DST confirmation, the patient's name, registration number and other vital information must be entered into the MDR-TB Suspect Register prior to sample transportation.
- Two sputum specimens for culture and DST should be collected in two separate specimen bottles for each patient. Instructions for the collection of a quality sputum specimen apply equally to culture samples as they do samples for smear microscopy (see Section 3.6).
- Ideally, specimens should be collected before TB treatment starts or as soon as possible thereafter.
- For culture and DST, the LTI should liaise with the reference laboratory for sample collection to confirm successful receipt of the sample by the reference laboratory and again after 8 weeks to request the results of culture and DST if they have not already been communicated.
- It is the responsibility of the LTI and focal TB clinician to follow-up with all patients to communicate culture and DST results and to start patients with positive results on appropriate anti-TB therapy determined by the drug susceptibility pattern.

Responsibilities of the nurse

- In the cases of hospitalised patients or where a LTI is not available, the ward nurse or TB focal nurse should distribute sputum collection bottles and collect sputum specimens from the patients (see Section 3.6).

Responsibilities of laboratory personnel for culture and DST confirmation

- Ensure that screw caps are fixed tightly to prevent leakage of sputum during transportation.
- Ensure the specimen bottles are properly labelled with the patient's name, date and suspect/culture registration number.
- Store sputum awaiting culture securely under refrigerated conditions (between 2 – 8^{O} C—do NOT freeze) and away from sunlight while awaiting transportation to the referral laboratory.
- Pack sputum specimens in an NTP/CRL-approved cooler box along with the corresponding specimen request forms. The transport/cooler box must be leak-proof and durable and have space to hold culture and DST laboratory request forms. Laboratory personnel should ensure that specimens for culture and DST reach the TB Reference Laboratory within 4 days of collection. To do so, laboratory personnel should deliver sputum specimens to the approved specimen courier service,

8.7 Treatment of multidrug-resistant TB.

Multidrug-resistant TB is treated with second-line TB drugs for a minimum period of 20 months. However, the standardised treatment regimen is as follows:

TABLE 8.2 Drugs used in the standardized treatment of MDR-TB

First line oral agent	Pyrazinamide (Z)
Injectables	Kanamycin (Km), Amikacin (Am)
Fluoroquinolones	Moxifloxacin (Mfx)
Second line oral bacteriostatic drugs	Prothionamide (Pto), P-aminosalicylic acid (PAS)

MDR-TB will be managed at DR-TB treatment centres until they are culture-negative. Thereafter treatment will continue within the community through a network of health care providers and treatment supporters.

The following IC measures are recommended in the care of all patients with MDR-TB:

- Isolation for all hospitalized patients with MDR-TB;
- Use of surgical masks by the patients in the presence of others;
- Use of N95 masks by health workers and visitors, where possible;
- Allowance of adequate ventilation in the patient or clinical encounter room and, where possible, placement of patients in rooms with abundant sunlight; and
- Restriction of patient movement—until the patient is documented to be doing well

on treatment the patient should voluntarily refrain from visiting indoor spaces where others could be newly exposed to the resistant TB.

9 TB infection control (IC)

TB IC should be implemented within the scope of general infection prevention at each health facility.

9.1 Management intervention

- Strengthen the existing infection prevention coordinating body to include TB IC.
- All health facilities should have an infection control committee responsible for developing a written infection control plan, monitoring its implementation and providing effective training for health care workers and other staff. Each health facility should appoint one person to serve as the infection control coordinator. This person should also oversee TB IC.
- Every health care worker should be trained in TB IC.
- HIV-positive health care workers should not work in high- risk areas, including TB wards, general medical wards and TB suspect/patient waiting areas such as TB clinics, MDR-TB clinics, cougher triage areas, etc. Encourage all health care workers to undergo HIV testing and counselling (HTC).

9.2 Administrative interventions

- Recognize TB suspects early and expedite the diagnostic process.
- Separate TB suspects and patients from other patients in congregate areas.
- Collect sputum in designated areas, ideally with ample ambient UV radiation (e.g. sunlight) and ventilation.
- Triage TB suspects to more quickly access diagnostic services (e.g. establish facility-based TB Walk-in Centres).
- Encourage cough etiquette for TB suspects and patients and, where possible, providing surgical masks to all hospitalised TB suspects.

9.3 Environmental interventions

- *Natural ventilation*: ensure that all areas of the working healthcare environment (e.g., OPD, consultation rooms, wards, HTC rooms, clinic, laboratory etc.) are well ventilated. Open windows and doors to ensure maximum natural ventilation.
- *Mechanical ventilation*: ensure that ceiling fans, air- conditioners and exhaust fans are in good working condition.
- *Ultraviolet germicidal irradiation* (UVGI): ensure that the lamps are cleaned and monitored weekly. Install UVGI lamps in open clinical areas to ensure maximal radiation coverage. Lamps should be left switched on continuously for 24 hours per day. UV bulbs should be replaced every 6 months.

9.4 Personal Protective Equipment (PPE)

Certified N95 or greater respirators are recommended for health workers when in close contact with infectious TB patients or working in high risk areas like MDR-TB wards, TB wards, general medical wards, TB reference laboratories or when conducting aerosol-

producing procedures (like inducing sputum). The respirator should be properly fitted in order to provide maximum protection. An N95 respirator can be reused several times provided that the mask holds its shape.

10 Health Promotion

10.1 TB health education

Health education is a key contributor to the NLTP's goals. This strategy is used across all aspects of TB control, from case finding to treatment. Advocacy is used to make sure that TB services are a consistent priority at every level and that resources are available and allocated accordingly. Case finding requires that health workers and the community be aware of the signs and symptoms of TB and that TB suspects be able to easily access TB diagnostic services. Health promotion enhances early case detection and treatment with all the benefits these confer to improving treatment outcomes.

Health workers attending to patients at outpatient departments in every health delivery setting should be very familiar with TB as a disease as well as common TB diagnostic procedures. Health workers should ensure that frequent health education sessions are conducted in all OPD departments by the LTI, focal clinician, focal nurse or the Health promotion Officer.

Communication devices such as TVs and radios can supplement the information provided during health education sessions. Health education drama groups, available at the hospitals, can also be used to provide TB information whilst the patients are waiting for a diagnosis.

The Information, Education, and Communication (IEC) Officer, in coordination with the TB Officers, is charged with the responsibility to develop a list of topics or themes for the routine health education sessions performed at the hospital.

TB education should start immediately after a suspect is diagnosed with TB. The TB Officers, the TB focal nurse, the TB focal clinician and the DTOs are responsible for educating patients about TB. Each health worker should exhibit exemplary inter- personal communication skills and form a strong patient-provider relationship in order to promote patients' adhering to anti-TB treatment and following medical advice.

10.2 Key TB and TB/HIV messages

- TB is a disease caused by germs.
- TB is spread from one person to another through coughing or sneezing.
- The major symptom of TB of the lungs is coughing.
- It is important for TB patients to take all the prescribed TB drugs as scheduled for the whole duration of treatment to avoid drug resistance..
- To prevent the spread of TB, it is important for patients
  - To report to the health facility as soon as they notice symptoms,
  - Always cover their mouths and nose when coughing or sneezing.
- Each patient has a choice to receive DOT services at the nearest health facility
- All smear-positive patients must have follow-up sputum smear examinations after 2, and 5 months of anti-TB treatment.
- TB patients on treatment should report any adverse drug reactions to a health worker

at the nearest health facility.
- It is important for TB patients to eat a well balanced diet and to avoid alcohol and tobacco.

In addition to the above key messages, TB patients must be given information about and be tested for HIV:

- Some people with TB have HIV as well. It is important to get tested for HIV.
- TB is curable even when the patient is co-infected with HIV. Benefits of testing for HIV include ART and co-trimoxazole preventive therapy for those TB patients found to be HIV positive.

All HIV-positive TB patients should be referred to the ART clinic immediately after diagnosis of HIV infection. The LTI should discuss HIV testing with all TB patients who have not been tested for HIV in the last 3 months. All HIV-positive patients at the HTC, ART and HIV care clinics should be screened for TB through the use of a 4-symptom questionnaire. Apart from at the TB ward and TB office waiting area, IEC on TB should also be given at the OPD, HTC, ART and reproductive and child health (RCH) clinics. Having adequate and correct information about TB is important since health workers are the primary sources of TB information for TB suspects, patients and the community. Provision of TB information to TB patients should be done regularly. IEC materials should supplement facility-based health talks. After the one-on-one interaction with a newly diagnosed TB patient, the LTI should make sure that TB education continues through sessions done on all the TB wards twice weekly. To supplement information dissemination, the LTI should routinely invite different ex-TB patients to provide moral support to current patients. Former patients may serve as an important source of information for current patients by sharing their experiences living with and overcoming the disease.

The TB ward chairperson should be provided with information on TB and should be counselled on how to provide this information to fellow patients and their guardians on a daily basis.

The LTI should make sure that they always coordinate with the district IEC officers when conducting health education sessions with all the target groups.

11 Managing medicines and other supplies

11.1. Role of general health care worker in drug and logistics management at the Regional Level

At the regional level, the regional store keeper is responsible for:

- Ensuring that stock cards are opened for all drugs and other commodities
- Documenting all transactions and updating all stock cards correctly and regularly
- Signing delivery voucher for drugs and other commodities
- Filing all records and reports for drug and other commodity management
- Making request for the regional drugs/supplies based on need and the quarterly statistics
- Checking that the drug usage correspond to drug supplied to the facility
- Conducting physical inventory monthly for all commodities

11.2 Patient kits

WHO advocates the use of FDCs for first-line TB treatment because these medicines significantly reduce a patient's pill burden and can significantly improve adherence levels. Drug supply to the district level will be carried out on quarterly basis based on need. The number of patients detected in a particular quarter is used to determine the requirements for the next.

11.3 Determining Quantities of TB drugs and recording and reporting formats

It is important to ensure that enough drugs are in stock for all TB patients expected to start treatment during the next quarter (all categories of treatment). It is assumed that the number of new patients in each treatment category next quarter will be the same, or approximately the same, as it was in the previous quarter. At the beginning of each quarter, the RLTCO focal person should determine these numbers from records of current cases and will order drugs according to the steps below:

- Establish the number of TB patients treated last quarter for each treatment category.
- Estimate the average monthly consumption by dividing the quantity issued within the previous quarter by 3.
- Multiply the average monthly consumption by 5 to determine maximum stock quantity required for a quarter.
- Determine the physical inventory (stock on hand) by checking the quantity of each of the drugs in stock (in the store).
- Deduct the physical inventory from the maximum stock quantity to determine the quantity to order

Quantity to order= Maximum stock quantity - stock on hand

The NLTP forms on estimation and ordering of drugs and supplies should be used to

quantify and order supplies.

11.4. Use and management of supply box

Each kit is designed for patient within the standard weight band of 38- 54kg. In the event of a patient with weight outside this range, an adjustment is required.
Do the following:

- Take a full (complete) Stop TB kit
- On the outside of the kit, write: **Supply Box**
- Any extra blisters you removed when adjusting the patient boxes can be placed in the **Supply Box**
- Any additional blisters you need for adjusting the kits, you can take from the **Supply Box** according to the schedule in table below

Patient KIT for new cases

Table 11.1: Patient KIT for new cases

	Patient weight			
	30-37kg	38-54kg	55-70kg	>70kg
RHZE(blisters)	Remove 2	No change	Add 2 blisters	Add 4 blister
RH	Remove 4 blisters	No change	Add 4 blisters	Add 8 blisters

Patient KIT for retreatment cases

Table 11.1: Patient KIT for re-treatment cases

	Patient weight			
	30-37kg	38-54kg	55-70kg	>70kg
RHZE(blisters)	Remove 3	No change	Add 3 blisters	Add 6 blister
RHE(blisters)	Remove 5 blisters	No change	Add 5 blisters	Add 10 blisters

- Be careful to always place the blisters on the correct side of the *Supply Box***,** so as not to mix RHZE or RHE blisters. When a *Supply Box* is empty, prepare a new *Supply Box* as described above, discarding the old one
- Any blister sheets remaining inside patient kits from patients who have defaulted, died or were transferred out should also be placed in the Supply Box and used for adjusting other patient kits in your TB centre, unless instructed otherwise by your supervisor or the NTP Guidelines.
- Open stock cards to manage individual drugs (RHZE, RH, RHE, Streptomycin, etc) for the supply box

In some cases the treatment of a category I patient may extended in the intensive phase by an additional 1 month for a total of 3 months of RHZE, rather than the normal 2 months. For these patients do the following:

	Patient weight			
	30-37kg	38-54kg	55-70kg	>70kg
RHZE(blisters)	Add 2 blisters	Add 3 blisters	Add 4 blisters	Add 6 blisters

11.5 Good Storage and Management Procedures for Drugs and Other Medical Supplies

Health facility drugs and other medical supplies are kept in the health regional drug storeroom, which should be well kept and managed by a designated responsible staff member. Good storage and management procedures are important for anti-TB drugs. (

11.5.1 Stock Management

- Stocks of anti-TB drugs are kept safe in the main storeroom, which should be locked when not in use.
- Drugs and other commodities should not be kept directly on the floor
- Ensure that fire prevention measures are implemented.
- The temperature, light and humidity in the main storeroom should be kept moderate by increasing ventilation, , and repairing any roof leaks quickly.
- Storage conditions can be improved by some simple measures using fans, air vents or windows to increase ventilation, Direct light can be prevented from entering the room by hanging curtains or painting the window glass.
- No one should eat, drink or smoke in the storeroom. Do not keep food or drink in the storeroom. This will help to keep the storeroom clean and free of pests and rodents.
- Stocks of anti-TB drugs in the storeroom (in individual patient drug boxes or stocked by type of drug) should be placed on shelves by expiry date: the drugs that expire soonest should be in front and those that expire later should be behind.
- When taking drugs off the shelf, use those expiring first (First-to- expire, First-out (FEFO)
- Return expired drugs or excess stock to the RLTCO for onward transmission to the regional pharmaceutical stores using the combined requisition and issue note book .
- Maintain a stock cards/tally cards for each drug and each strength and this should be kept next to that drug on the shelf.

11.6 Completing the Stock Card/Tally Card

The stock card is a stock keeping record that is used to track supplies received, issued and held in storage. When properly filled, the stock card helps to determine the stock level of a commodity at any point in time. This card is very important in the NLTP Commodities Logistics Management System provides important information for completing the daily and monthly consumptions, Quarterly Reports, Quantifications, Requisitions and Issuance. It is therefore important that data entering into this form should not be neglected; neither should it be delegated to lower level personnel without regular supervision. Any errors in this card affect the entire supply chain system, which can lead to under or over estimation. This card is generally kept at the store and there is one stock card for each item. These drugs are further managed using drug account book at the facilities.

12 Monitoring and Evaluation

12.1 Programme Supervision

The NLTP should ensure sustenance of task-oriented supervision at all levels to increase the efficiency of health workers by developing their knowledge, perfecting their skills, improving their attitudes towards their work and increasing motivation. The NLTP Central Unit should

provide technical supervisory support to the health regions, while the regional health teams (RHTs) in turn supervise health facilities.

The emphasis of supervision to the regions should be on supporting the regional health officers in technical and managerial functions, while that of facilities should focus on identification of TB cases and administration of treatment including follow up of cases.
Supervisory visits must be planned carefully. Before each visit the supervisor should review the health centre's reports, the correspondence about the reports, the findings of the last supervisory visit and corrective actions already taken.

Supervision should be conducted using the appropriate supervisory tools such as supervisory checklist that assesses the relevant tasks. The facilities to be visited should be notified in advance of the date and purpose of the visit. The number of visits should be planned before the start of the fiscal year, for inclusion in the annual-programme budget.

12.2 Programme monitoring

12.3.1 Calculating indicators

It is important to monitor the success of TB case detection and treatment activities. This involves

- Keeping good records at the health facilities
- Reviewing health facility records regularly
- Compiling data
- Analysing key indicators related to TB case detection and treatment.

The following records are used for the calculation of the indicators:

a. TB suspect register
b. TB Central register
c. VCT register
d. TB lab register
e. Drug account book
f. Summary forms (quarterly drug assessment form, quarterly treatment outcome, sputum conversion, monthly case notification form & cohort forms for enablers)

An indicator is determined by dividing a numerator (top number) by a denominator (bottom number) to obtain a proportion. It may be expressed as a percentage if multiplied by 100.

12.3.2 Analyzing indicators

It is not just enough to calculate indicators. Analysis and interpretation of the data must be done.

- Comparing the actual proportion achieved with the expected or desired proportion.
- Comparing results achieved from one quarter to the next.
- It is helpful to keep a line graph of the facility performance on the wall

12.4 Reporting and Recording system

Table 12.1: Recording and reporting formats used in the National TB Programme

S/No.	M&E format	Data requirement	Level	Responsible	Frequency of entry
1	TB Suspects (chronic cough) register	Records of patients presenting with chronic cough	Health facility	General Health Care staff	Daily
2	Sputum Examination request form	Results of AFB smear microscopy	Health facility	General Health Care staff	Daily
3	TB Laboratory register	Results of AFB smear microscopy	Laboratory	Laboratory Scientist or technician	Daily
4	TB Culture/ Sensitivity Request/Report	Request for DST	Laboratory-NRL	Laboratory Scientist or technician	Based on need.
5	TB Treatment Card	Patients treatment records and progress	Health facility	LTI's	Daily
7	TB Transfer Form	Patient's up to date treatment status	Health facility	LTI's	Based on need.
9	Health facility TB Central register	Records of all TB cases in an district	Regional/National	LTI	Weekly /Monthly
10	Health facility monthly Case notification form	Report on TB cases detected in a month by category.	Regional /National	LTI	Monthly and annuallyQuarterly, Annual
11	Quarterly Report on Sputum Conversion form.	Report on treatment outcome of TB cases started on treatment 3-6 months earlier.	Regional /National	LTI's and RLTCO	Quarterly, and Annual
12	Quarterly treatment out come TB Cohort Report form.	Report on treatment outcome of TB cases started on treatment 12-15 months earlier.	Regional /National	RLTCO and LTI	Quarterly, and a Annual
13	Quarterly TB drugs assessment form.	Quarterlyhealth facility drug assessment form	Regional /National	LTI's & RLTCO	Quarterly, and Annual

S/No.	M&E format	Data requirement	Level	Responsible	Frequency of entry
14	Pharmcovigilance reporting forms	Monthly reporting forms	Regional and health facility	LTI's and RLTCO	Monthly

Annexes

1. Reporting and recording formats