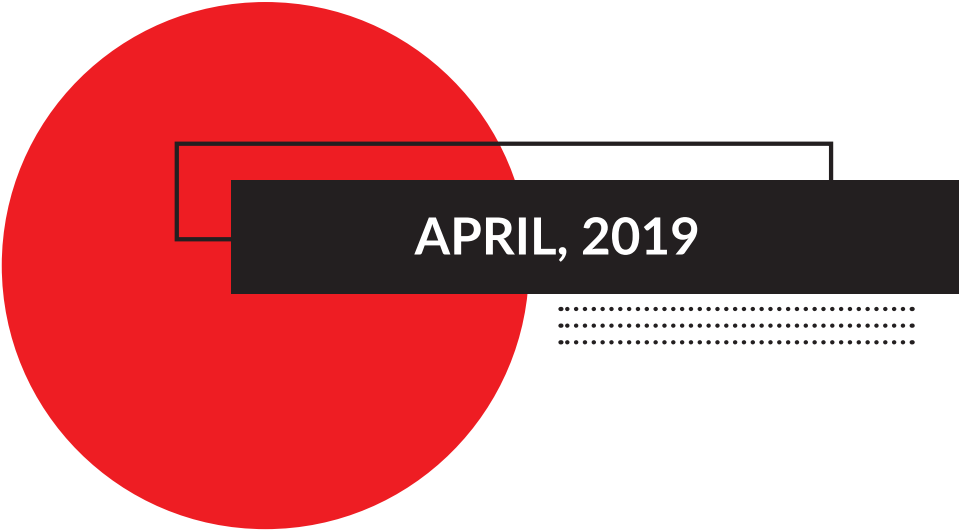


Guidelines For **Latent Tuberculosis Infection** Management in Ghana



APRIL, 2019



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Guidelines For
**Latent Tuberculosis
Infection**
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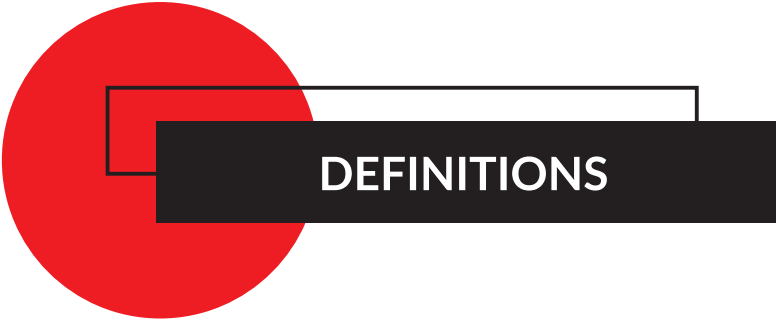
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ABBREVIATIONS

ART	Antiretroviral treatment
BCG	Bacille Calmette-Guérin
CI	Confidence interval
CLHIV	Children Living with HIV
CPT	Co-trimoxazole Preventive Therapy
DR-TB	Drug-Resistant TB
DOTS	Directly Observed Treatment Short Course
DST	Drug Sensitivity Testing
ICF	Intensified Case Finding
IGRA	Interferon-Gamma Release Assay
IPT	Isoniazid Preventive Therapy or Treatment
LTBI	Latent Tuberculosis Infection
MDR-TB	Multidrug-Resistant Tuberculosis
PLHIV	People Living with HIV
SOPs	Standard Operating Procedures
TPT	Tuberculosis Preventive Therapy
TST	Tuberculin Skin Test
TB	Tuberculosis



DEFINITIONS

The definitions listed below apply to the terms as used in these guidelines.

Adult: A person over 19 years of age

Adolescent: A person aged 10–19 years.

Child: A person under 10 years.

Infant: A child under 1 year of age.

Bacteriologically confirmed TB: TB diagnosed in a biological specimen by smear microscopy, culture or a WHO-approved molecular test such as Xpert MTB/RIF.

Close contacts of TB (including DRTB) patients: People living in the same household as the index patient, or spending many hours a day together with the patient in the same indoor space.

Due to the difficulty in tracing contacts of TB clients, contact investigation should be integrated into routine programmatic management of TB and DR-TB

Contact: Any person who was exposed to a case of TB (see definition below).

Contact investigation: A systematic process for identifying previously undiagnosed cases of TB among the contacts of an index case. In some settings, the goal includes testing for LTBI to identify candidates for preventive treatment. Contact investigation consists of identification and prioritization and clinical evaluation.

High-TB-incidence country: A country with a WHO-estimated TB incidence rate of $\geq 100/100\,000$.

Household contact: A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of current treatment.

Index case (index patient) of TB: The initially identified case of new or recurrent TB in a person of any age, in a specific household or other comparable setting in which others may have been exposed. An index case is the case on which a contact investigation is centred but is not necessarily the source case.

Latent tuberculosis infection (LTBI): A state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. There is no gold standard test for direct identification of *Mycobacterium tuberculosis* infection in humans. The vast majority of infected people have no signs or symptoms of TB but are at risk for active TB disease.

Preventive treatment: Treatment offered to individuals who are considered to be at risk for TB disease in order to reduce that risk. Also referred to as LTBI treatment or preventive therapy.

Tuberculosis (TB): The disease state due to *Mycobacterium tuberculosis*. In this document, commonly referred to as “active” TB or TB “disease” in order to distinguish it from LTBI.



EXECUTIVE SUMMARY

Tuberculosis (TB) is the most common opportunistic infection with a high mortality rate among HIV-infected individuals. The risk of TB in HIV-infected persons continues to increase as HIV disease progresses and immunity decreases. There are persons who are HIV negative but are at risk of developing TB disease by virtue of having immunosuppression from medications or disease. It has been found that a vast majority of people infected with TB do not have no signs or symptoms of TB but are at high risk of active TB disease when the immune system becomes compromised. This state is known as Latent TB infection (LTBI) and is defined as 'a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB(1).

TB Preventive Therapy (TPT) is the administration of one or more anti-tuberculous drugs to individuals with latent TB infection to prevent progression to active disease. WHO recommends the use of Isoniazid for 6 months in resource-limited settings for the prevention of TB in at-risk populations living in high TB incidence, prevalence and transmission settings. The use of Isoniazid is one of the ways in which active TB disease is prevented among at-risk populations in high TB incidence settings. Others include Rifampicin and Isoniazid taken daily for 3 months and Rifapentine plus Isoniazid weekly for 3 months.

Among PLHIV, preventing TB entails the 3 'I's: Intensified case finding, Isoniazid Preventive Therapy (IPT), Infection Control for TB plus early initiation of ART. The risk of developing TB disease is reduced by about 60-90% in individuals who are given TPT.

The development of the TB Preventive Therapy Guidelines for Ghana is a milestone in the response towards improving management of TB/HIV co-infection and prevention of TB in those who are HIV-negative but are at high risk of developing TB disease.



CHAPTER 1

1.1 INTRODUCTION

Tuberculosis (TB) is the most frequent cause of AIDS-related deaths worldwide, despite progress in access to ART(2). It caused about 400,000 deaths among people living with HIV in 2016, representing one third of all HIV deaths. Global data in 2016 indicated that people living with HIV were 21 times (2,3) more likely to develop active TB than those without HIV infection(4). There is a fourfold increase in the number of TB cases registered by national TB programmes, due to the dramatic spread of the HIV epidemic throughout sub-Saharan Africa in the past years.

Based on the WHO Global End TB Strategy which includes the objective to reduce TB incidence by 90% by 2035, the National HIV/AIDS Control Programme (NACP) and National TB Programme (NTP) have set out the interventions needed to achieve the interim objective of reducing TB transmission among the most vulnerable populations.

1.11 BACKGROUND

Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB (5).

As there is no “gold standard” test for LTBI, the global burden is not known with certainty. However, up to one third of the world’s population is estimated to be infected with *M. tuberculosis* (6–8), and the vast majority have no signs or symptoms of TB disease and are not infectious, although they are at risk for active TB disease and for becoming infectious. Several studies have shown that, on average, 5–10% of those infected will develop active TB disease over the course of their lives, usually within the first 5 years after initial infection (9). The risk for active TB disease after infection depends on several factors, the most important being immunological status (5). Among children, active TB after infection is highest in the first year of life. Children younger than one year have a 40% risk of developing active TB disease if infected as compared to the general population who have only a 10% lifetime risk of reactivation to active disease (10). Tuberculosis (TB) is a major cause of morbidity and mortality in people living with HIV (PLHIV) (11); it can accelerate the course of HIV infection and decrease the survival of patients with AIDS (12). TB mortality rates are significantly higher for PLHIV (RR=9), and early detection reduces the chances of mortality (13, 14). Prevention of active TB disease by treatment of LTBI is therefore a critical component of the WHO End TB Strategy (15).

The efficacy of currently available treatments for LTBI ranges from 60% to 90% (2). The potential benefit of treatment should, however, be carefully balanced against the risk for drug-related adverse events. Mass or population-wide LTBI testing and treatment are not feasible because the tests are imperfect, there are risks of serious and fatal side-effects, and the cost would be high, for a strategy of unproven public health impact. For infected individuals in population groups with high risk for progression to active disease compared to the general population the benefits outweigh the harm. Management of LTBI involves a comprehensive package of interventions: identifying and testing those individuals who are exposed, delivering effective, safe treatment in such a way that the majority of those starting a treatment regimen will complete it with no or minimal risk of adverse events. The process should be monitored and evaluated to assess the outcomes.

1.12 RATIONALE

The 2015 prevalence of TB in Ghana was 282 per 100,000 and the incidence, 156 per 100,000 (16). This places Ghana in a high TB incidence category (high TB incidence estimated annual TB incidence rate, ≥ 100 per 100 000 population) (5). Given this background, management of LTBI is recommended for children and adults living with HIV (17) and contacts (adult and children) of people with TB and other clinical risk groups living in settings with a low TB incidence (estimated annual TB incidence rate < 100 per 100 000 population) (5, 18, 19). There are other at-risk persons who also benefit from LTBI treatment. These include patients with solid organ and haematological transplant, anti-tumour necrosis factor (anti-TNF) treatment, those on dialysis and those with silicosis.

Current WHO guidelines on LTBI is based on the probability that the condition will progress to active TB disease in these specific risk groups, the underlying epidemiology and burden of TB, the availability of resources and the likelihood of a broader public health impact. The WHO recommendations and guidelines led to a significant increase in preventive treatment of TB particularly among people living with HIV but the global coverage of this intervention is still very low (4).



CHAPTER 2

2.0 IDENTIFICATION OF POPULATIONS FOR TESTING AND TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI)

Not all individuals infected with *M. tuberculosis* develop active TB. It is estimated that the lifetime risk of an individual with LTBI for progression to active TB is 5–10%(9). The risk is particularly high among children under the age of 5 years and among people with compromised immunity(5).

As preventive treatment entails risks and costs, preventive treatment of *M. tuberculosis* infection should be selectively targeted to the population groups at highest risk for progression to active TB disease and who would benefit most from treatment of LTBI.

Programmatic management of LTBI should select treatment that offers lasting protection for the at-risk population. A critical component of programmatic management should therefore be a comprehensive individual clinical assessment that considers the balance between the risks and benefits.

2.1 ADULTS AND ADOLESCENTS LIVING WITH HIV (AALHIV)

Adults and adolescents living with HIV, who are unlikely to have active TB should receive preventive treatment of TB as part of a comprehensive package of HIV care. Treatment should be given to these individuals irrespective of the degree of immunosuppression; also to those on antiretroviral treatment (ART) who are not virally suppressed, those previously treated for susceptible TB and pregnant women.

2.2 INFANTS AND CHILDREN LIVING WITH HIV (CLHIV)

With special consideration of on-going transmission of TB (Ghana being a high TB incidence country), the following apply:

- All Infants and children living with HIV who are in contact with a case of TB and are investigated for TB should receive 6 months of TB preventive treatment (TPT) if the investigation shows no evidence of TB disease.
- All infants and children living with HIV in whom TB disease has been ruled out and who have no contact with a case of TB should be offered 6 months of TPT as part of a comprehensive package of HIV prevention and care
- All infants and children living with HIV who have been successfully treated for TB may receive a course of preventive treatment if there is a high risk of re-infection or recurrence. Preventive treatment can be started immediately after the last dose of TB therapy or later, according to clinical judgement.

2.3 HIV-NEGATIVE HOUSEHOLD CONTACTS OF A PERSON WITH PULMONARY TB

With special consideration of on-going transmission of TB, the following apply:

- HIV-negative children aged less than 5 years who are household contacts of people with pulmonary TB and who are found not to have active TB after clinical evaluation should be given TB preventive treatment
- Children aged 5 years or more, adolescents and adults who are household contacts of people with pulmonary TB who are found not to have active TB after clinical evaluation may be given TB preventive treatment.

2.4 OTHER HIV-NEGATIVE AT-RISK GROUPS

Patients who fit the following criteria should be screened and treated for LTBI:

- Anti-Tumour Necrosis Factor treatment,
- Patient receiving dialysis,
- Patients preparing for or who have had solid organ or haematological transplant and
- Patients with silicosis

It is recognized that people with diabetes, people with harmful use of alcohol, tobacco smokers and underweight people are also at risk of developing TB. However, the benefits of systematic, routine testing and LTBI treatment of these at-risk people do not outweigh the risks, unless they are part of the groups covered in the recommendations.

2.5 PEOPLE WHO SHOULD NOT BE GIVEN TPT

- Patients with symptoms of TB should be fully evaluated to rule out TB disease before they can be eligible for IPT
- People with active TB disease
- PLHIV previously treated for MDR TB
- MDR TB contacts
- Known or suspected hypersensitivity to Isoniazid
- Chronic liver disease or hepatitis
- Regular or heavy alcohol consumption
- Moderately severe peripheral neuropathy.
- History of convulsions and psychosis
 - Concomitant medication- phenytoin, carbamazepine, selective serotonin re-uptake inhibitors, antidepressants, oral ketoconazole, itraconazole, warfarin, theophylline, disulfiram

Testing for Latent TB Infection in PLHIV (adults and paediatrics)

Note: Testing for latent TB (using Tuberculin Skin Test (TST) or Interferon Gamma Release Assays (IGRAs)) is not required before offering TPT.

All PLHIV (paediatric and adults) should be offered TPT immediately active TB has been ruled out.

JOB AIDS ON IDENTIFICATION OF AT-RISK POPULATIONS FOR LTBI TESTING AND TREATMENT

ELIGIBILITY FOR TPT

1. All PLHIV who screen negative for TB irrespective of ART status
2. All HIV negative children under 5 years who have contact with a smear positive TB case and screen negative for TB.
3. Patients receiving dialysis, anti-TNF treatment, solid organ and haematological transplant patients (both pre and post-transplant) and those with silicosis
4. Persons living with HIV who have successfully completed their TB treatment

CONTRAINDICATIONS FOR TPT

- Patients with symptoms of TB need to be screened to rule out TB with TB screening tool
- Patients with active TB
- PLHIV previously treated for MDR-TB
- Known or suspected hypersensitivity to isoniazid
- Alcohol use (regular and harmful)
- Chronic liver disease or symptoms of hepatitis (self-reported, right upper quadrant pain, dark urine, yellowing of the eyes (jaundice), pale stools)
- History of convulsions (exclude febrile convulsion in children)
- History of psychosis
- Moderately severe peripheral neuropathy (burning sensation in the limbs)
- Concomitant use of phenytoin, carbamazepine, warfarin, theophylline, disulfiram, SSRIs, antidepressants (citalopram, fluoxetine, paroxetine, sertraline), oral ketoconazole or itraconazole

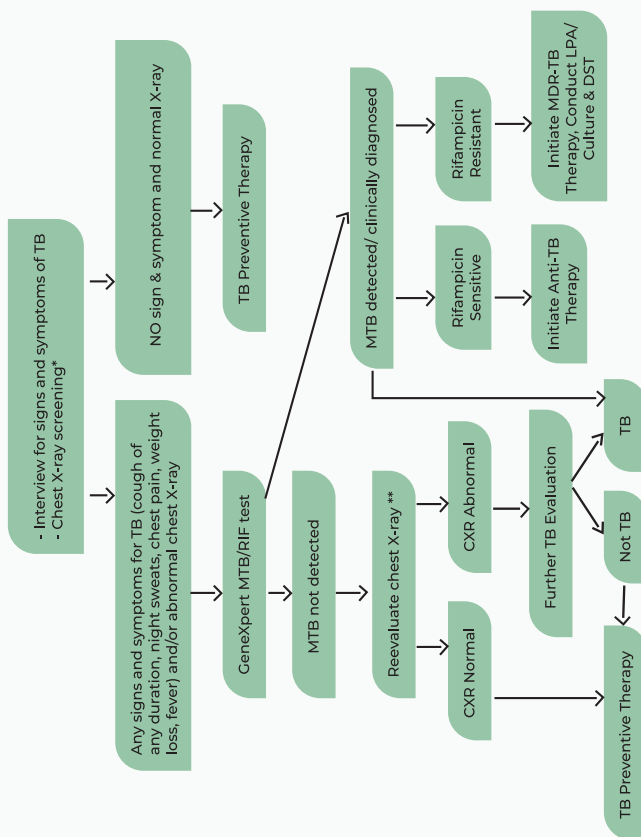


3.1 ALGORITHMS FOR RULING OUT ACTIVE TB DISEASE

Introduction

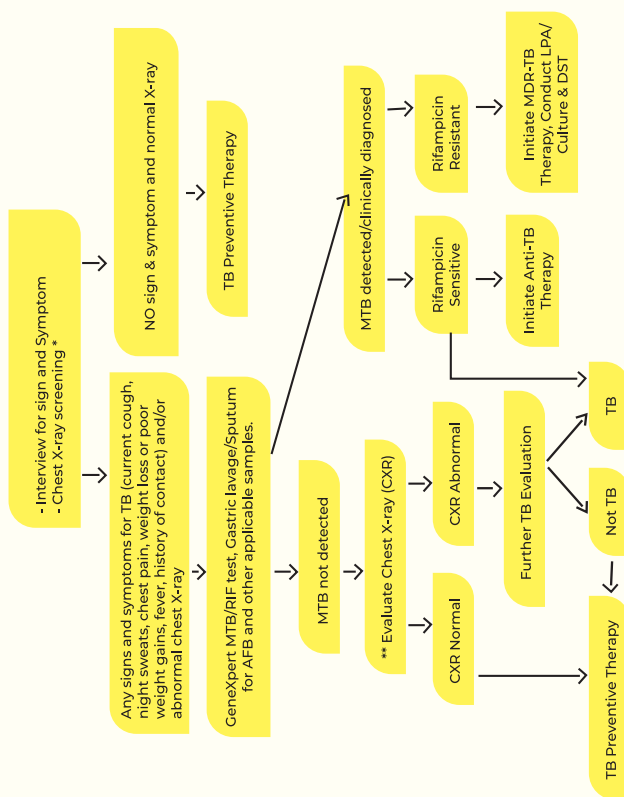
It is necessary to rule out active TB in a patient before starting TPT. The following algorithms are to be followed to facilitate the exclusion of active TB. Where asterix (*) are indicated it implies further investigations are required by a health care worker with a higher expertise to ensure TB is ruled out and other conditions are not missed. It is recognized that some facilities may not have the digital Chest-X-Ray facilities provided by the NTP. The absence of this should not be a barrier for implementing these algorithms.

ALGORITHM FOR SCREENING AND DIAGNOSIS OF TB IN PLHIV



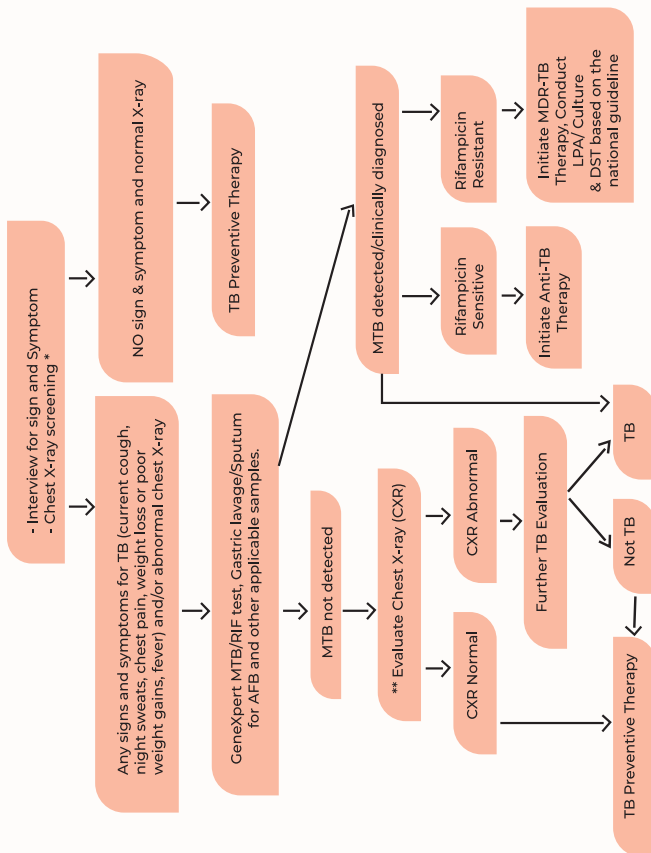
**X-ray used to screen, ** X-ray used as diagnostic tool*

ALGORITHM FOR SCREENING AND DIAGNOSIS OF TB IN CHILDREN LIVING WITH HIV



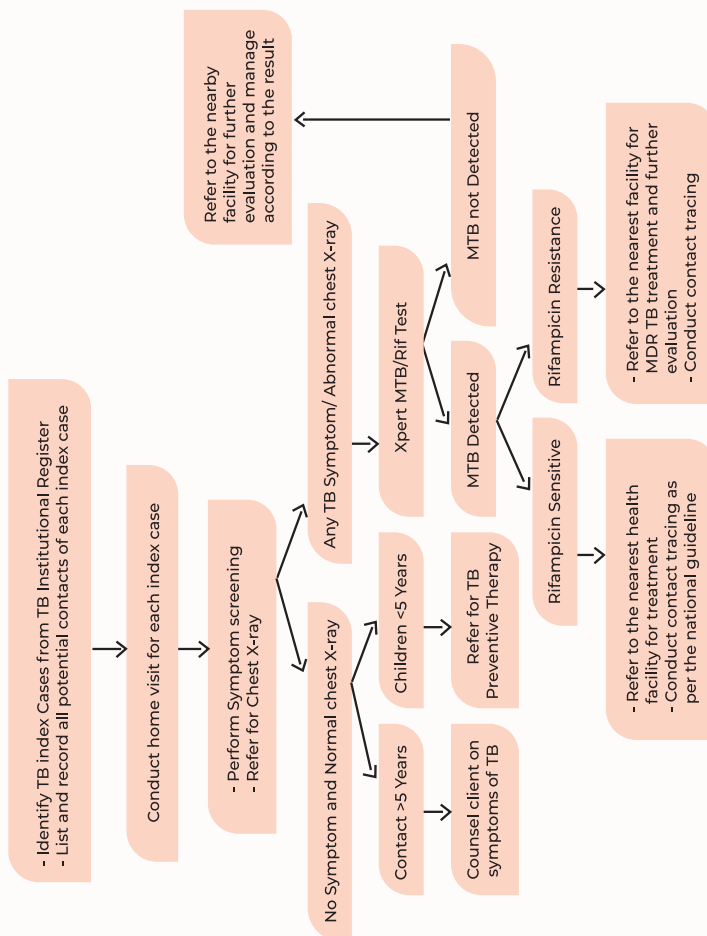
**X-ray used to screen, ** X-ray used as diagnostic tool*

SCREENING & DIAGNOSIS OF TB IN CHILDREN IN CLOSE CONTACT WITH TB PATIENT



*x-ray used to screen, ** X-ray used as diagnostic tool*

GENERAL APPROACH FOR TB CONTACT TRACING



3.2 SOPS FOR SCREENING OF TB AND IMPLEMENTATION OF TPT IN PLHIV

WHO should be screened?

All people living with HIV need to be screened for HIV in each visit using symptom screening tool and minimum two times a year using both symptom and X-ray screening.

Steps for screening

1. For all clients living with HIV register the client name on the TB screening tool and ask if the client has any of the TB symptoms listed on the screening tool: ask if a client is coughing and duration; ask if client has chest pain, weight loss, night sweat and fever. On the screening tool tick all symptoms that has been reported yes by a client.
2. If a client does not have any of the TB symptoms and has never been screened using X-ray more than 6 months, fill X-ray request form and send the patient for chest X-ray screening.
3. Evaluate screening result. For any client presenting with abnormal chest X-ray or at least one of the TB symptom (cough, chest pain, weight loss, night sweat or fever) mark as eligible for sputum examination and proceed to investigate using GeneXpert or Sputum Smear microscopy (eligibility criteria section B). Please escort the patient to the lab to ensure sputum submission
4. For any client responding NO to all TB symptoms and has normal chest X-ray mark as not eligible for sputum examination. If a client had never been on TB preventive therapy (TPT), counsel the client and put on TPT.
5. If the client diagnosed with TB (clinically or bacteriologically confirmed) refer a patient to DOTS center for TB treatment.

SYMPTOMS BASED SCREENING TOOL (CHEST INFECTION)											
Region: _____ District Name: _____		Health Facility/ Community Name: _____									
SCREENING SITE a. General OPD ☐ b. HIV/ART Clinic ☐ c. ANC/Reproductive Health ☐ d. Male Ward ☐ e. Female Ward ☐ f. Paediatric Ward ☐ g. Diabetic Clinic ☐ h. Household Contact Tracing ☐ i. Prisons ☐ j. Community ☐ k. Other Specify: _____											
Who is eligible for sputum examination? A. Facility based screening (excluding People Living with HIV)* • Cough >2 weeks with or without additional symptom • Cough<2 weeks with at least one other TB symptom • Abnormal chest X-ray with or without symptom B. People Living with HIV** • Any one or more TB symptoms • Abnormal Chest X-ray with or without symptom C. Contact tracing or Community Based Screening** • Abnormal Chest X-ray with or without symptom • Any one or more TB symptoms Evaluate screening result and send client to laboratory for sputum examintaion if ELIGIBLE for TB testing		SYMPTOMS Cough more than 2 weeks Cough less than 2 weeks Chest Pain Weight Loss Night Sweats Fever		X-RAY SCREENING X-ray examination not done Normal Chest X-Ray Abnormal Chest X-Ray eligible for sputum examination Other abnormalities not eligible for sputum		ELIGIBILITY FOR LAB TEST Eligible: Presumed TB case (Suspect) Non Eligible: Other Lung Disease Non Eligible Known TB case: counsel and provide guidance		REMARKS			
		Date of Screening									
		DD/MM/YY									
		SEX M F									
		AGE									
		NAME									

3.3 SOPS FOR SCREENING AND DIAGNOSING TB IN CHILDREN LIVING WITH HIV

- Child visits the facility (Paediatric clinic, ART Center, TB Center, and or ART /TB Collaborative centre)
- Screen child using TB symptom screening tool including history of contact with TB patient or patient with chronic cough and X-ray.
- For a “yes” response to any of the signs and symptoms (ie cough of any duration, night sweat, chest pains, weight loss/ poor weight gain, fever, history of contact with TB patient or patient with chronic cough) or abnormal X-ray do GeneXpert test
- If MTB is detected;
 - Initiate anti TB therapy if Rifampicin is sensitive.
 - If Rifampicin resistant refer to regional MDR TB
- For a child who tests negative for MTB :
- Reevaluate chest x-ray
 - If chest X-ray is abnormal refer the child to TB expert for further evaluation.
 - If chest X-ray is normal, initiate the child on TPT.

3.4 SOPS FOR SCREENING AND DIAGNOSING TB IN HIV-NEGATIVE CHILDREN < 5 YEARS WHO ARE HOUSEHOLD CONTACTS OF PEOPLE WITH PTB.

- Screen child using TB symptom screening and Chest X-ray
- If a “yes” response to any of the symptoms (i.e. cough of any duration, night sweat, chest pains, weight loss/ poor weight

gain, fever, history of contact with TB patient or patient with chronic cough)

or

abnormal X-ray conduct GeneXpert test.

- If MTB is detected;
- Initiate anti TB therapy if Rifampicin is sensitive.
 - If child is Rifampicin resistant refer to regional MDR TB
- For a child who tests negative for MTB:
- Reevaluate the chest x-ray.
 - If chest X-ray is abnormal refer the child to TB expert for further evaluation.
 - If chest X-ray is normal, initiate the child on TPT.



CHAPTER 4

4.1 TREATMENT OPTIONS FOR LATENT TUBERCULOSIS INFECTION

- Isoniazid monotherapy for 6 months is recommended for treatment of LTBI in both adults and children.
- Rifapentine and isoniazid weekly for 3 months may be offered as an alternative to 6 months of isoniazid monotherapy as preventive treatment for both adults and children.
- Rifampicin and isoniazid daily for three months.

Recommended dosages of drugs for the treatment of LTBI

Drug Regimen	Dose	Maximum Dose
Isoniazid alone, daily for 6 months	Adults, 5 mg/kg Children, 10 mg/kg	300 mg
Weekly rifapentine* plus isoniazid for 3 months (12 doses)	Individuals aged ≥ 12 years: Isoniazid: 15 mg/kg Individuals aged 2–11 years: isoniazid: 25 mg/kg Rifapentine: 10.0–14.0 kg = 300 mg 14.1–25.0 kg = 450 mg 25.1–32.0 kg = 600 mg 32.1–50.0 kg = 750 mg > 50 kg = 900 mg	Isoniazid, 900 mg Rifapentine, 900 mg

* Regimens containing rifapentine should be prescribed with caution to PLHIV who are on PI-based ART & Nevirapine-based ART because of potential drug–drug interactions.

Special Circumstances

Patients previously treated for TB (<i>Secondary prophylaxis</i>)	All PLHIV who have successfully completed treatment for TB disease should receive TPT for an additional six months. TPT can be started immediately after the last dose of anti-TB therapy or at a later date.
Patient on TPT develops TB during TPT treatment	If patient develop TB symptoms during IPT treatment do the following: 1. Evaluate patients for TB. Do DST for isoniazid, rifampicin, aminoglycosides and fluoroquinolones where available. Treat according to resistance pattern. 2. If no resistance, treat for normal TB.
IPT in children born to smear positive mothers:	If a baby is born to a mother with TB (irrespective of type of TB), assess the newborn for TB. Non-specific features suggestive of neonatal TB include: Fever, low birth weight, hepato- splenomegaly, irritability, feeding intolerance. If the child has none of the above, give IPT for 6 months. Withhold BCG until 2weeks after completion of IPT.
IPT and MDR-TB	Contacts of MDR TB and PLHIV with DR TB are not eligible for IPT.

4.2 DOSAGE SCHEDULE FOR TREATMENT OF LATENT TB INFECTION

DOSAGE SCHEDULE

Isoniazid monotherapy for 6 months is recommended for treatment of LTBI in both adults and children in Ghana.

Dose of INH for TPT **CHILDREN**

Weight Range (kg)	Dose in mg	Number of 100mg tablet	Number of 300mg tablet
< 5	50	½ tablet	Not recommended
5.0 -9.9	100	1 tablet	Not recommended
10.0-13.9	150	1 ½ tablet or	½
14.0-19.9	200	2 tablets	Not recommended
20.0-24.9	250	2 ½ tablets	Not recommended
≥25	300	3 tablets or	1 tablet

Dose of INH for TPT **ADULTS**

Weight Range (kg)	Dose in mg	Number of 100mg tablet	Number of 300mg tablet
20-30	150	1 ½ tablet	½ tablet
31-40	200	2 tablets	-
>40	300	3 tablets	1 tablet

Rifapentine and Isoniazid weekly for 3 months may be offered as an alternative to 6 months of isoniazid monotherapy as preventive treatment for both adults and children in Ghana.

Dose of Rifapentine plus Isoniazid

Drug Regimen	Dose	Maximum Dose
Weekly Rifapentine plus isoniazid for 3 months(12doses)	Individuals aged ≥ 12 years: Isoniazid: 15mg/kg Individuals aged 2-11 years: Isoniazid: 25mg/kg Rifapentine: 10.0 -14.0 kg = 300mg 14.1 - 25.0 kg = 450mg 25.1- 32.0 kg = 600mg 32.1- 50.0 kg = 750mg >50kg = 900mg	Isoniazid, 900mg Rifapentine, 900mg

NB:

Rifampicin- and rifapentine-containing regimens should be prescribed with caution to people living with HIV who are on ART because of potential drug–drug interactions. Administering them at secondary and tertiary facilities where possible is therefore preferred.

- Clients on Dolutegravir (DTG) should take it twice daily instead of once daily when on Rifampicin containing regimen.

All clients who are on TPT should also receive Pyridoxine.

Dosages for Pyridoxine

Weight Range(kg)	Dose in mg	Number of 100mg tablet	Number of 300mg tablet
<25	25	1 ½ tablet	½ tablet
≥ 25	50	1 tablets	½ tablet

In special circumstances, kindly follow the table below;

SCENARIO	ACTION(S)
Patients previously treated for TB (<i>Secondary prophylaxis</i>)	All PLHIV who have just successfully completed treatment for TB disease should receive INH for an additional six months. • All PLHIV who have been successfully treated for TB and are living in settings with a high TB prevalence and transmission should receive TPT for an additional six months at the same doses above. TPT can be started immediately after the last dose of anti-TB therapy or at a later date
Patient on TPT develops TB during TPT treatment	• Stop TPT • Treat patient for TB • Administer TPT for 6 months after the TB treatment
TPT in children 0-5 years with contact with smear positive patients	• Administer TPT for 6 months after ruling out active TB disease



5.1 GUIDE FOR MONITORING CONTACTS OF TB CLIENTS

‘Close contacts’ of TB (including DRTB) patients are defined as people living in the same household as the index patient, or spending many hours a day together with the patient in the same indoor space. Due to the difficulty in tracing contacts of TB clients, contact investigation should be integrated into routine programmatic management of TB and DR-TB.

5.2 GROUPS TO BE INVOLVED IN CONTACT MONITORING

Patient. Contact investigation starts with the education of the TB patient. Patients should be educated about the infectiousness of their disease and the high risk of transmission to contacts who share the same living space. While they should not be unduly alarmed, they should be informed that their family members are likely already infected with TB, so the most important intervention is to monitor them closely for symptoms of active TB.

Family. One of the most important reasons to do a home visit for every TB patient at the initiation of TB treatment is to do contact investigation. A community nurse or health care provider should educate the family that they are all likely already infected with TB, and explain the importance of notifying the community or clinical team quickly about family members who develop symptoms of active TB.

Clinical team. The clinical team has multiple opportunities to inquire about the health of the TB patient's family contacts. At every clinical evaluation, doctors and nurses should ask the patient whether any family member has developed TB symptoms.

Community nurses or health care providers educated on TB. During home visits to check adherence or assess the social situation, the community nurse should inquire if there are any family members who have developed symptoms of active TB. The community nurse may also directly interview the family members at their home. Community nurses are also best suited to address fears or doubts about the health system or other social barriers to treatment for TB contacts.

Community volunteers: community volunteers, who are the closest to the family and are most likely to identify family members with TB symptoms can be involved in contact tracing. This is particularly true for members of the extended family who visit periodically.

5.3 DIAGNOSTIC WORK UP FOR ADULTS WITH TB SYMPTOMS

1. An evaluation by a healthcare provider, including history and physical examination;
2. A chest xray

3. Sputum investigations (ideally a rapid diagnostic method such as Xpert MTB/RIF, or if not available, sputum smear microscopy; culture and drug susceptibility testing (DST))
 4. HIV testing.
- If the initial investigation is not suggestive of active TB, the household contact should continue to be monitored closely by the clinical team.

5.4 DIAGNOSTIC WORK UP FOR PAEDIATRIC CONTACTS WITH TB SYMPTOMS

1. An evaluation by a healthcare provider, including history and physical examination
2. A chest xray
3. Tuberculin skin testing with purified protein derivative (older child due to effect of BCG)
4. Sputum investigations (ideally a rapid diagnostic method such as Xpert MTB/RIF, or if not available, sputum smear microscopy; culture and DST)
5. HIV testing
 - * Follow algorithm for household contacts found to be negative for active TB.
 - * There is no need for TPT in close contacts of MDRTB clients



CHAPTER 6

6.1 MONITORING OF ADVERSE EVENTS

Definitions:

Adverse Event

An adverse event is a medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related.

Adverse reactions

A response to a drug which is noxious and unintended, and which occurs at doses normally used in individuals for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function.

Adverse reactions have been associated with isoniazid use (asymptomatic elevation of serum liver enzyme concentrations, peripheral neuropathy and hepatotoxicity) Rifampentine (cutaneous reactions, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity).

Reviews

HIV negative clients receiving TPT should be monitored routinely at monthly visits.

PLHIV receiving TPT should be monitored at their regular ART review visits.

Health care providers should explain the rationale of the treatment, importance of completing it and the possible side effects and actions to be taken.

Patients receiving TPT should be advised to contact their health care provider at anytime if they become aware of symptoms such as;

- Anorexia (lack of appetite for food)
- Nausea
- Vomiting
- Abdominal discomfort
- Persistent fatigue or weakness
- Paraesthesia and numbness

Advise clients receiving TPT to stop the treatment and immediately report to the health facility if they experience any of the following symptoms:

- Dark-coloured urine
- Pale stools
- Yellowing of the eyes (Jaundice)
- Significant abdominal pain
- Convulsions

Health care providers should advise clients put on TPT to volunteer information on medication history if they experience any of the above listed symptoms but present to a health facility other than the facility where TPT was initiated.

Evaluate patient, do a liver function test and manage appropriately.

NB: Health providers should remember to complete the Adverse Drug Reaction form.

6.2 JOB AIDE ON MONITORING ADVERSE EVENTS

Adverse reactions have been associated with isoniazid (asymptomatic elevation of serum liver enzyme concentrations, peripheral neuropathy and hepatotoxicity) and rifapentine (cutaneous reactions, hypersensitivity reactions, gastrointestinal intolerance and hepatotoxicity) use.

Reviews

- HIV negative clients receiving TPT should be monitored routinely at monthly visits.
- PLHIV receiving TPT should be monitored at their regular ART review visits.
- Explain to the client the rationale of TPT, importance of completing it, possible side effects and actions to be taken.
- Advise patients receiving TPT to report to the health facility at any time if they become aware of symptoms such as;
 - Anorexia (lack of appetite for food)
 - Nausea
 - Vomiting
 - Abdominal discomfort
 - Persistent fatigue or weakness
 - Numbness of the limbs
- Advise clients on TPT to stop treatment and report immediately to the health facility if they experience the following symptoms:
 - Dark-coloured urine
 - Pale stools
 - Jaundice
- Advise clients on TPT to volunteer information on their medication history if they experience any of the above listed symptoms but present to a health facility other than the facility where TPT was initiated.

- Evaluate patient who reports with any of the above symptoms, do a liver function test and manage appropriately.
- **NB: Complete the Adverse Drug Reaction forms and give to appropriate person responsible as early as possible**



CHAPTER 7

7.1 ADHERENCE TO AND COMPLETION OF PREVENTIVE TREATMENT

It is important to educate patients on the TB disease process, rationale and benefits of TPT. Strict adherence to and compliance with TPT is essential for the patient to achieve the benefit of TPT. Adherence should be assessed and reinforced at every visit. Screen clients for active TB using the algorithm for screening and diagnosis of TB at every visit.

7.2 JOB AIDE

Adherence to and completion of preventive treatment

- Explain the reason and benefit of TPT to the client
- Educate client of the dosage and duration of TPT
- Educate client on side effects and what to do
- Assess adherence by patient self-report and/or pill count at every visit
 - If there is evidence of non-adherence, explore the reason and counsel accordingly

- If patient discontinue for <1mth, assess, counsel and continue
 - If patient discontinue for >1mth, assess, counsel and investigate for active TB then restart TPT if patient show commitment
 - If patient discontinue for more than 3mths or more than once, do not reinitiate
- Screen for active TB among all clients at every visit using the Tb screening tool
 - If TB is found, Stop TPT and treat
- At the end of the 6mth inform client that TPT has been completed and congratulate client
 - Educate the client report to the clinic with any signs and symptoms of TB



8.1 MONITORING AND EVALUATION

Surveillance of TPT implementation will be done using the indicators below. The district health coordinators (for TB, HIV or TB/HIV collaborative programmes) will submit data on monthly and quarterly basis to district and national management teams. The reports will contain but are not limited to the national indicators set.

Indicator	Numerator	Denominator	Purpose	Source
Number of PLHIV newly enrolled in HIV care		N/A	To help with projections and forecasting of commodity needs	Monthly summary form for ART
Number of PLHIV screened for TB		N/A	To help with projections and forecasting of commodity needs	Monthly summary screening tool
Number of PLHIV newly enrolled in HIV care screened for TB		N/A	To help with projections and forecasting of commodity needs	Monthly summary screening tool
Number of PLHIV newly enrolled who are eligible for TPT		N/A	To help with projections and forecasting of commodity needs	Monthly summary screening tool
Number of PLHIV newly enrolled in HIV care started on TPT		N/A	To help with projections and forecasting of commodity needs	Monthly summary form for ART
Total number of PLHIV newly enrolled who received and completed TPT				DHIMS
Proportion of PLHIV newly enrolled in HIV care screened for TB	Number of PLHIV newly enrolled in HIV care screened for TB	Number of PLHIV newly enrolled in HIV care	Measure the capacity of the programme to detect active TB among PLHIV	DHIMS

Indicator	Numerator	Denominator	Purpose	Source
Proportion of PLHIV newly enrolled who are eligible and received TPT	Number of PLHIV newly enrolled who are eligible and received TPT	Number of PLHIV newly enrolled who are eligible for TPT	Measure the capacity of the programme to initiate TPT among PLHIV	DHIMS
Treatment completion rate	Total number of PLHIV newly enrolled who received and completed TPT	Total number of PLHIV newly enrolled who were initiated on TPT 9 months ago		
Total number of children under 5 who are household contacts of PTB cases screened		NA	To help with projections and forecasting of commodity needs	Monthly summary screening tool
Total number of children under 5 who are household contacts of PTB cases		NA	To help with projections and forecasting of commodity needs	DHIMS
Total number of children under 5 who were eligible and received TPT		N/A	To help with projections and forecasting of commodity needs	DHIMS
Total number of children under 5 who were eligible for TPT		N/A	To help with projections and forecasting of commodity needs	DHIMS

Indicator	Numerator	Denominator	Purpose	Source
Total number of children under 5 who are household contacts of PTB cases who were screened	Total number of children under 5 who are household contacts of PTB cases who were screened	Total number of children under 5 who are household contacts of PTB cases	Measure the capacity of the programme to detect active TB among children <5 who are household contacts of PTB cases	DHIMS
Proportion of children under 5 who are household contacts of PTB cases who were eligible and received TPT	Total number of children under 5 who were eligible and received TPT	Total number of children under 5 who were eligible for TPT	Measure the capacity of the programme to initiate TPT among children <5 who are household contacts of PTB cases	DHIMS
Total number of children under 5 who received and completed TPT		N/A		DHIMS
Treatment completion rate	Total number of children under 5 who received and completed TPT	Total number of children under 5 who were initiated on TPT 9 months ago		DHIMS
Total number of eligible individuals in at risk populations tested for LTBI		N/A	To help with projections and forecasting of commodity needs	DHIMS
Total number of eligible individuals in at risk populations tested for LTBI and received TPT		N/A	To help with projections and forecasting of commodity needs	DHIMS

Indicator	Numerator	Denominator	Purpose	Source
Proportion of eligible individuals in at risk populations tested for LTBI and received TPT	Total number of eligible individuals in at risk populations tested for LTBI and received TPT	Total number of eligible individuals in at risk populations tested for LTBI	Measure the capacity of the programme to detect active TB among eligible individuals in at risk populations	DHIMS
Proportion of eligible individuals in at risk populations tested for LTBI and received TPT and completed the TPT	Total number of eligible individuals in at risk populations tested for LTBI and received TPT and			DHIMS



BIBLIOGRAPHY

1. WHO. WHO | Latent TB Infection: Updated and consolidated guidelines for programmatic management [Internet]. WHO. World Health Organization; 2018 [cited 2018 May 6]. Available from: <http://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/>
2. Ford N, Matteelli A, Shubber Z, Hermans S, Meintjes G, Grinsztejn B, et al. TB as a cause of hospitalization and in-hospital mortality among people living with HIV worldwide: a systematic review and meta-analysis. J Int AIDS Soc [Internet]. 2016 [cited 2018 May 6];19(1):20714. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26765347>
3. Gray DM, Workman LJ, Lombard CJ, Jennings T, Innes S, Grobbelaar CJ, et al. Isoniazid preventive therapy in HIV-infected children on antiretroviral therapy: a pilot study. Int J Tuberc Lung Dis [Internet]. 2014 Mar 1 [cited 2018 May 6];18(3):322-7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24670570>
4. World Health Organization-WHO. World Health Organization, Annual TB Report 2017. SEARO [Internet]. 2018 [cited 2018 May 6]; Available from: http://www.searo.who.int/tb/documents/annual_tb_repot_2017/en/

5. Getahun H, Matteelli A, Abubakar I, Aziz MA, Baddeley A, Barreira D, et al. Management of latent *Mycobacterium tuberculosis* infection: WHO guidelines for low tuberculosis burden countries. *Eur Respir J* [Internet]. 2015 Dec [cited 2018 May 6];46(6):1563–76. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26405286>
6. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, et al. The Growing Burden of Tuberculosis. *Arch Intern Med* [Internet]. 2003 May 12 [cited 2018 May 6];163(9):1009. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12742798>
7. Dodd PJ, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Heal* [Internet]. 2014 Aug [cited 2018 May 6];2(8):e453–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25103518>
8. Houben RMGJ, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. Metcalfe JZ, editor. *PLOS Med* [Internet]. 2016 Oct 25 [cited 2018 May 6];13(10):e1002152. Available from: <http://dx.plos.org/10.1371/journal.pmed.1002152>
9. Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. *Am J Epidemiol* [Internet]. 1974 Feb [cited 2018 May 6];99(2):131–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/4810628>
10. Loeffler M. *Ann. Pediatric Clinical Advisor - Instant diagnosis and Treatment*. 2nd Ed. 2007. edited by Garfunkel CL, Kaczorowski MJ, Christy C.
11. WHO (2004) Recommendations of the Interim Policy on Collaborative TB/HIV activities. *Wkly Epidemiol Rec* 79: 6–11.

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